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Intrathoracic Neurogenic Tumors[1]

KARL KORNBLUM, M.D., and HOWARD H. BRADSHAW, M.D.

Philadelphia

THE CHEST IS THE acknowledged diagnostic province of the roentgenologist. This is particularly true of tumors within the thoracic cavity. Clinical symptoms and physical signs are often few and slight and are frequently entirely lacking. It is astounding how great a size a tumor within the chest may attain before giving rise to symptoms. The fact that many such tumors are more or less accidentally discovered in routine roentgen examinations is, of course, well known. Thus, it is generally agreed that roentgen examination is the best means of detecting intrathoracic neoplasms.

The detection of a chest tumor upon the roentgenogram is a relatively simple matter. To determine its nature, however, often affords considerable difficulty. Since the shadows produced by such lesions all more or less resemble one another, differentiation becomes a perplexing problem. Treatment and prognosis are, of course, largely dependent upon the nature of the tumefaction and a precise diagnosis is therefore of the utmost clinical importance. There are certain clinical and roentgenologic features which serve to distinguish one tumor from another, and a critical analysis of the roentgenograms correlated with the clinical aspects of the case will often serve to establish a correct diagnosis. All too frequently, however, both the clinical and roentgenologic data are too meager to permit of a positive diagnosis, and one must be content to consider the most likely possibilities. The roentgenologist should never dismiss such a case merely with the diagnosis of mediastinal or pulmonary tumor. Such a report is of only limited clinical value. Even in the absence of symptoms and physical signs, the law of probability and such factors as age, sex, and location of the tumor should enable the roentgenologist to suggest the most likely possibility as regards the nature of the lesion.

Tumors occurring within the chest are numerous and varied both in their clinical and roentgen manifestations and this adds materially to the difficulty of diagnosis. Among the more common intrathoracic tumefactions are primary carcinoma of the bronchi and lungs, metastatic tumors of a large variety, lymphoblastomas, such as Hodgkin's disease and lymphosarcoma, and aneurysms of the thoracic aorta. Aside from these, there is a large variety of tumors less frequently encountered. In this latter group belong the neoplasms of neurogenic origin that form the basis of this report, the purpose of which is to bring these tumors before the roentgenologist, to direct attention to their relative frequency and their variable occurrence within the chest, and to emphasize

[1] From the Departments of Radiology and Surgery, Jefferson Medical College and Hospital, Philadelphia, Penna. Read before the Radiological Society of North America at the Twenty-sixth Annual Meeting, Cleveland, Ohio, Dec. 2–6, 1940.

the clinical and roentgenologic features by means of which they may be recognized.

The classification and pathology of neoplasms of neurogenic origin, especially those of the peripheral nerves, have afforded much opportunity for controversy. Consequently, as in many fields of pathology, confusion and disagreement exist regarding the nature and pathology of many neurogenic tumors occurring outside the central nervous system. Furthermore, the multitude of names that have been applied to neurogenic tumors of different types adds to the difficulty of any attempt at an orderly and coherent understanding of the subject. The neophyte in this field becomes involved in a maze of terminology and pathology from which he finds it difficult to extricate himself. While it was originally intended to classify and give a brief description of the tumors of the peripheral nerves, the difficulty of the task and the fact that most of such tumors have no direct bearing upon the subject at hand caused this idea to beaban doned. Suffice it to say that all tumors considered in this report, with the exception of one metastatic lesion included because of its similarity to the others, have been identified by histologic study as of neurogenic origin. A brief pathologic description of several of the tumors is included in the case reports. It has been difficult in each individual case to determine the nerve of origin of the lesion, whether a peripheral nerve of the central nervous system, or the sympathetic system. From the standpoint of roentgenologic recognition, as well as the therapeutic management of the case, this seems to be of secondary importance.

CLINICAL MANIFESTATIONS

There appears to be no age or sex predilection of these tumors as they occur in the chest. The clinical manifestations are in most instances not very striking. The onset of symptoms is usually insidious, although at times they may come on rather abruptly. Since the tumors may be either benign or malignant, the rapidity of the clinical course is largely dependent upon this factor. The symptoms are chiefly those of pressure, and since the lesion may occur in any part of the chest, the symptomatology will depend upon the structures upon which pressure is exerted. It seems correct to say that the majority of neurogenic tumors occur in the posterior part of the chest, well away from any of the vital structures in the mediastinum. Here they may attain considerable size before giving rise to pressure manifestations. As a matter of fact, the neurogenic tumors constitute some of the largest neoplasms occurring in the thoracic cavity.

Among the more constant and prominent symptoms are pain in the chest and cough. One or other of these may predominate, but it is seldom that either is absent. The pain varies in character from a sharp stabbing type to a dull ache and as a rule is worse at night. There is usually radiation from the point of greatest intensity in the chest to some neighboring structure such as the upper abdomen. Possibly because of their rapid growth, malignant lesions give rise to more pain than benign ones. Radiation to the shoulder on the side of the lesion is quite characteristic. The cough is usually of a chronic nature and may or may not be accompanied by expectoration. Loss of weight is the next most common symptom, being more evident with the malignant lesions. With involvement of the recurrent laryngeal nerve aphonia may occur, while dysphagia will appear if the esophagus is implicated. With a tumor in the mediastinum, especially the anterior portion, dyspnea is a prominent symptom; the patient may complain of a sense of pressure beneath the sternum, and cyanosis may at times be quite evident. Fever is usually an indication of infection occurring as a complication, usually as a result of bronchial obstruction.

Physical signs, usually quite marked because of the size which these tumors attain, are those of replacement of normal air-bearing lung tissue by a solid tumor. There are flatness to percussion and an ab-

sence of breath sounds directly over the tumor. The surrounding lung tissue may present evidence of compression. The heart and mediastinum may be displaced away from or toward the tumor, depending upon whether the latter is large enough to push these structures toward the opposite side or whether the existence of an atelectasis, from bronchial obstruction, causes a shift toward the lesion. Mediastinal pressure may manifest itself by dilatation and engorgement of the vessels of the neck and upper chest. There may be physical signs in the abdomen in the form of a readily palpable liver, spleen, or kidneys, due to downward pressure by large tumors just above the diaphragm.

Laboratory studies are for the most part negative. A secondary anemia will be present in the malignant lesions or in the terminal stages of a benign tumor. A leukocytosis usually means infection, especially when accompanied by fever.

Complications are common. Because of their size, many of these tumors cause interference with normal pulmonary physiology by pressure. Interference with lung drainage and the occurrence of atelectasis invite infection. Symptoms of this complication may dominate the clinical picture and in some instances are responsible for the patient seeking medical attention. Atelectasis is more prone to occur with tumors arising in the mediastinum, permitting the larger bronchi to be compressed. This is likewise true of pleural effusion, which is occasionally encountered. Phrenic nerve paralysis is also a manifestation of a mediastinal origin of the tumor. Spinal cord symptoms may be present, but can hardly be regarded as a complication, since in these instances the tumor has its origin within the vertebral canal, from which it emerges by way of an intervertebral foramen—the so-called "dumb-bell tumor." Any evidence of an intrathoracic tumor in these cases is merely a secondary manifestation. It is possible, however, for a tumor to arise in the chest and project into the vertebral canal.

ROENTGEN MANIFESTATIONS

The roentgen examination is by far the most important clinical investigation in these cases. Although the general nature of the disturbance may be suspected from the clinical signs and symptoms, a careful roentgen examination is usually required to establish the neoplastic nature, the exact size, and the location of the lesion. The roentgenologist must not be content with the revelation of these facts but must lend his art to the establishment of the possible histologic nature of the tumor. This can often be accomplished if the roentgen examination is thorough and properly correlated with the clinical aspects of the case. There are many pitfalls, however, which often lead to errors in roentgen diagnosis.

The roentgen investigation should consist of a careful fluoroscopic observation and an adequate roentgenographic study. The fluoroscopic examination is of the utmost importance, as it enables one to observe the effect of the tumor upon the respiratory and cardiac action, the position of the diaphragm, and its movements. The lesion should be studied with the patient in every conceivable position. This will make it possible to determine the positions for making films that will show the tumor to best advantage. In every case the esophagus should be visualized by means of an opaque medium and films made, which will determine whether it is directly or indirectly involved. An adequate number of pictures should be taken not only in the anteroposterior and lateral positions but in the oblique positions as well. With the neurogenic tumors, the lateral view is of particular importance and should never be omitted. The fact that these occur chiefly in the posterior part of the chest is of great diagnostic value, and this position of the tumor is best determined in the lateral projection. Stereoscopic films are often of value. Films made with the Potter-Bucky diaphragm should be a part of the routine study, as they may reveal details not seen in the ordinary chest roentgenograms.

Body section roentgenography may also be of considerable help in selected cases. The instillation of an iodized oil for bronchial visualization is not often required and is seldom of much diagnostic aid. Roentgen examination after the induction of an artificial pneumothorax will often give valuable information.

The roentgen appearance of the lesion depends upon the presence or absence of complications. In an uncomplicated case, the tumor usually presents itself as a well circumscribed, sharply defined spherical or globular mass. It is usually quite dense and homogeneous, standing out in sharp contrast to the surrounding lung. Although the lesion may occur in any portion of the chest, it is most commonly encountered posteriorly. This location, as pointed out above, is of considerable diagnostic aid and makes a lateral view of the chest imperative. In the lateral view, the tumor presents essentially the same dense, rounded, well circumscribed shadow as in the postero-anterior projection. The size of the neurogenic tumors is another of their diagnostic features. The fact that they become so large before detection indicates the benign character of the majority of these neoplasms.

Depending upon size and location of the tumor, the neighboring structures will show varying degrees of displacement. The diaphragm may be pushed downward; the heart, mediastinum, trachea, and esophagus will be displaced to the side opposite the tumor. Although the visualized esophagus may show a rather marked degree of displacement, it is only seldom that there is complaint of dysphagia. Apparently the slow growth of the tumor enables the esophagus to accommodate itself to its malposition.

With some complications, the characteristic features of an intrathoracic neurogenic tumor may be completely masked, making recognition extremely difficult or impossible. In the presence of an atelectasis the sharply defined circumference of the tumor may be partially or completely obliterated. The exact location and size of the lesion may not be readily appreciated. The shifting of the intrathoracic viscera incident to the atelectasis may further confuse the picture. When a pleural effusion occurs as a complication, the tumor may be completely hidden by the fluid, making recognition impossible. Aspiration of the fluid becomes necessary and the advisability of an artificial pneumothorax should be considered. This will show the lesion and may reveal sufficient evidence to warrant the diagnosis of a neurogenic tumor. With infection as a complication the entire process may be considered inflammatory in origin; the appearance roentgenologically may be that of a pneumonia.

DIFFERENTIAL DIAGNOSIS

In the differential diagnosis there are many intrathoracic tumefactions to be considered. The *lymphoblastomas*, Hodgkin's disease and lymphosarcoma, are confined to the mediastinum and usually produce in it a nodular enlargement. Lymphatic enlargements elsewhere in the body, from which a biopsy specimen can be taken, will serve to establish the diagnosis. The rather prompt and striking response of the lymphoblastomas to irradiation quite readily differentiates these lesions from the neurogenic tumors, which are highly radioresistant. When *lymphatic leukemia* involves the mediastinum it practically never does so as an isolated tumefaction. The blood picture reveals the true nature of this disease. An *aneurysm* of the thoracic aorta may closely simulate a neurogenic tumor. Usually its origin from the aorta can be established. The difference in the blood pressure in the two arms and a positive Wassermann reaction aid in the recognition of this lesion. A *dermoid cyst* presents the same dense, sharply demarcated shadow as a neurogenic tumor but is practically always located in the anterior mediastinum in contrast to the posterior position of the latter. A *thymoma* is confined to the mediastinum, is usually quite irregular in contour, and is located anteriorly. An *enlarged substernal thyroid*

is in a position seldom occupied by a neurogenic tumor; it compresses and causes deviation of the trachea and this with its anterior position and the clinical manifestations of thyroid disease serve to make the differentiation. A large, single, isolated *metastasis* such as is commonly seen in hypernephroma or teratoma of the testis may resemble a neurogenic tumor. The position of the lesion should aid in the differentiation in most instances. *Intrathoracic fibromas* and *lipomas* may not be distinguishable from a neurogenic tumor.

TREATMENT

The only treatment that is of any avail is the surgical removal of the tumor. When once the diagnosis has been established, no other form of therapy need be considered. Roentgen irradiation is of no value in the benign neurogenic tumors. In malignant lesions, it may give some temporary relief of symptoms. Important in the surgical attack upon the tumor is the accurate localization of the lesion so that the most adequate and advantageous approach may be made. This information is best obtained from a careful study of the roentgenograms.

Operation should be done under intratracheal anesthesia, since the pleura must be widely incised and as a rule there are few adhesions to prevent collapse of the lung. Usually one rib is resected and the posterior ends of one or more others are severed to obtain good exposure. The tumor usually arises in the postero-lateral portion of the thoracic wall and is easily removed by incising the parietal pleura about the base of the pedicle and gaining control of its blood supply. Removal may be difficult because of firm adherence to one of the lobes of the lung, to the mediastinum, to the pericardium, or to the diaphragm. In a recent case the tumor was densely adherent to both the lower lobe and the diaphragm so that a portion of the former had to be removed. (These adhesions probably result from pressure irritation and are, therefore, found most commonly with the larger tumors. On the other hand, if there is direct involvement of either the lung, diaphragm, mediastinum, or pericardium, it means that the lesion is one of the malignant neurogenic tumors.)

After removal of the tumor the chest is closed without drainage and the pneumothorax created by the operation is partially eliminated by needle aspiration. Serosanguineous fluid usually collects in the pleural cavity a few days after operation and should be aspirated. Frequent roentgen examinations of the chest are helpful in following the postoperative course for the development of complications and indications for therapy.

Certain of the neurogenic tumors project from the thoracic cavity through the intervertebral foramina into the spinal canal and produce cord symptoms (the so-called collar-button tumor). Under such circumstances a laminectomy should be performed in addition to the thoracic operation.

The patients are up and around in two to three weeks after operation. Usually the only residual evidence of the tumor is some diaphragmatic irregularity as a result of adhesions and a deformed, regenerated rib.

During the past four years seven intrathoracic neurogenic tumors have come under the writers' observation, as follows:

2 neurofibromas, removed surgically with excellent results.

1 neurofibroma, with sudden death from peritoneoscopy.

1 neurofibroma of the esophagus, with death four days after operation.

3 malignant neurogenic tumors.

(*a*) Exploratory thoracotomy and biopsy followed by roentgen therapy and death one year later.

(*b*) Death shortly after admission with no therapy; autopsy.

(*c*) Sudden complete paralysis from 4th thoracic level down. Exploratory thoracotomy and biopsy, with death three weeks later.

No evidence of metastases was found in any of these cases.

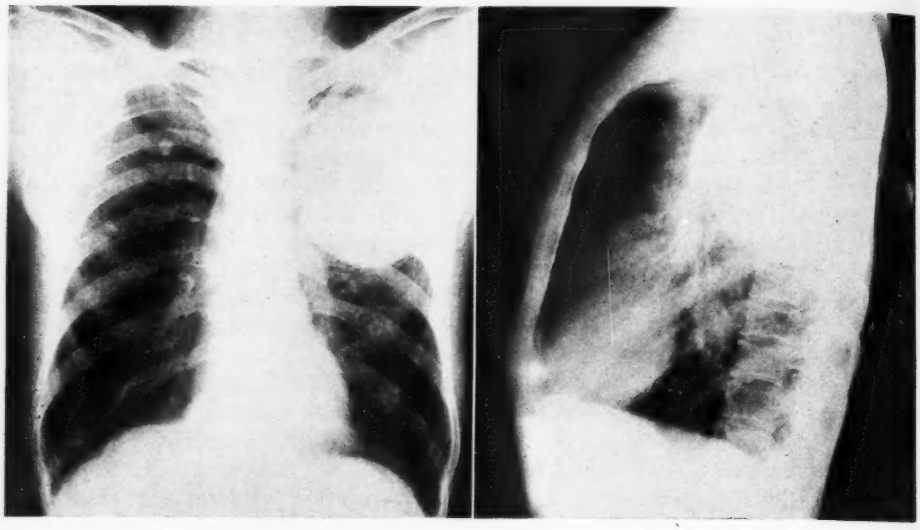


Fig. 1. Case 1: Characteristic appearance of a neurogenic tumor. The patient also has pneumoconiosis. The posterior position of the tumor in the lateral view is quite typical.

CASE REPORTS

CASE 1: *Typical Case.* L. R., white male, age 51, was admitted to Jefferson Hospital Oct. 7, 1936. His chief complaint was a chronic cough of four and a half months' duration and pain in the left shoulder.

The present illness began with a dry cough, worse when the patient was on his feet; it seemed to arise from something in the left chest. There had been a gradual but progressive loss of weight (25 lb.) and a marked feeling of fatigue. A roentgenogram was taken elsewhere, postural drainage was instituted, and for the first time since onset (three and a half months previously) the patient began to bring up sputum, sometimes as much as a tumbler full. It had no odor, was clear and mucinous, and occasionally blood-streaked.

Showing no improvement, the patient was referred to Jefferson Hospital. He was poorly nourished and examination showed signs slightly decreased over the anterior chest and practically absent from the 2nd to 6th ribs posteriorly on the left side. Fever averaged 100° F. and was of the intermittent type. The blood showed no leukocytosis but there was a mild secondary anemia. The sputum was negative. The clinical impression was (1) tumor of the lung, etiology questionable; (2) early bronchiectasis.

Roentgen examination on Oct. 10, 1936 (Fig. 1), showed a large rounded shadow occupying the greater portion of the left upper chest. It was very dense but from this examination alone it was difficult to say what the etiology might be. In the lateral view the lesion was seen to occupy the posterior half of the chest. The lungs showed evidence of a pneumoconiosis.

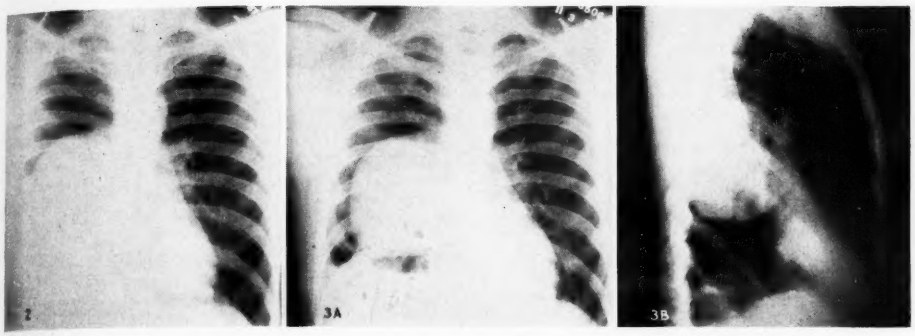
It was learned that the patient was born in German Poland in a sheep-raising district and since there was a 10 per cent eosinophilia the possibility of echinococcus cyst of the lung was suggested, but this diagnosis could not be confirmed.

Bronchoscopic examination showed a moderate displacement of the lower end of the trachea to the right, but no narrowing of the lumen. The tracheal displacement gave the impression that the left bronchus was displaced upward, but I do not believe that it was particularly influenced by the lesion in the left chest. There was no evidence of compression stenosis, no increase in secretion. From a bronchoscopic standpoint practically nothing abnormal was found.

Operation was performed on Oct. 23. A hard rounded tumor was found adherent to the posterior chest wall alongside the vertebrae at the 5th and 6th thoracic level. The tumor seemed to be invading both lobes of the lung. It was not possible to remove it, but a specimen was taken for histologic study. The pathologic report was malignant neurogenic tumor.

Following operation the patient was given a series of deep roentgen therapy. He showed continued improvement during the remainder of his stay in the hospital, and just before his discharge on Dec. 12, 1936, roentgen examination showed that the mass in the left upper chest was appreciably smaller than at the original examination. He was returned to the care of his family physician and died a year later from his malignant disease.

Comment: This case shows the typical roentgen appearance of the neurogenic



Figs. 2 and 3. Case 2: The lesion at the right base was obscured by a large pleural effusion, as shown in Fig. 2. After removal of the effusion, a well circumscribed tumor was visible, as shown in Figs. 3A and B.

tumors. Whether they are benign or malignant usually cannot be determined roentgenologically. Invasion of the lung found at operation is indicative of malignancy.

CASE 2: *Good Surgical Result.* W. G., white male, age 29, was admitted to Jefferson Hospital Nov. 1, 1937, with pain in the right lower chest and upper right abdomen present for one week before admission.

His present illness began with a sudden attack of severe, sharp, stabbing pain in the right chest, shoulder, and abdomen, accompanied by dyspnea and lasting for about three minutes. He went to see a doctor, who told him that he had a spasm of the diaphragm and gave him a hypodermic injection. He had had no previous attacks and had had no symptoms since then. There was no weight loss. The past medical history was entirely negative.

The patient was well nourished, showing no dyspnea or cyanosis. There was some limitation of expansion in the right lower thorax; vocal fremitus was absent over the right base up to the 6th rib in the scapular line with flatness and absence of breath sounds in the same area. All signs were present but somewhat diminished anteriorly. The left lung was normal. There was no fever and no abnormality in the blood picture. All laboratory studies were negative including the Wassermann and Kahn reactions. The clinical impression was pleurisy with effusion, right side; lung disease (?).

Roentgen examination, Nov. 3, 1937 (Fig. 2), showed a homogeneous area of density involving the lower half of the right chest. The upper border was convex and in the lateral view corresponded for the most part to the interlobar fissure. The picture was interpreted as an encapsulated interlobar collection of fluid. There was nothing to indicate the etiological factor. Following this the chest was aspirated and 16 ounces of bloody fluid were removed. A histologic study of this fluid revealed no tumor cells.

Roentgen examination following aspiration of the fluid (Fig. 3) showed a large spherical tumor occupying the middle and posterior portion of the right chest, arising from the mediastinal border. There was still some fluid remaining. The right lower lobe had been forced forward and was collapsed in its upper portion. The upper and middle lobes were essentially normal. *Interpretation:* Large cyst in the middle and posterior aspect of the right chest.

An aspiration biopsy of the tumor was done. Histologic study revealed no tumor cells or other definite tissue structures in either the fixed sediment or direct smear.

The patient refused operation and was discharged with a diagnosis of dermoid cyst or ganglioneuroma. He returned to the hospital Oct. 24, 1938. His health had been splendid in the interim and he had no complaints.

Roentgen examination was now reported as follows: The large tumor in the right side of the chest has increased considerably in size since the last examination. There is no fluid present in the pleural cavity. The chest is otherwise negative. *Interpretation:* Definite increase in size of neurofibroma of the right chest.

Operation was done Oct. 26, 1938. The right 8th rib was removed. A well rounded tumor was found, slightly adherent to the right middle and lower lobes, with a small pedicle attached to the postero-lateral chest wall in the region of the sympathetic chain.

The pathologic report, in part, is as follows: Specimen consists of a somewhat rounded, but slightly irregular mass which weighs 605 gm. and measures 12 × 10.5 × 9.5 cm. (Fig. 4). The mass seems to be encapsulated and the surface is fairly smooth, except for one place where fragments of connective tissue and muscle are attached. On section, the mass is solid with the exception of small cystic areas, which contain an amber-colored fluid and seem to be the result of degenerative changes in the tumor. The growth varies somewhat in consistency and is composed of a peculiar yellowish-gray tissue. Examination of sections reveals a definite fibrous capsule; just beneath the capsule in areas are numerous small nodules supported by

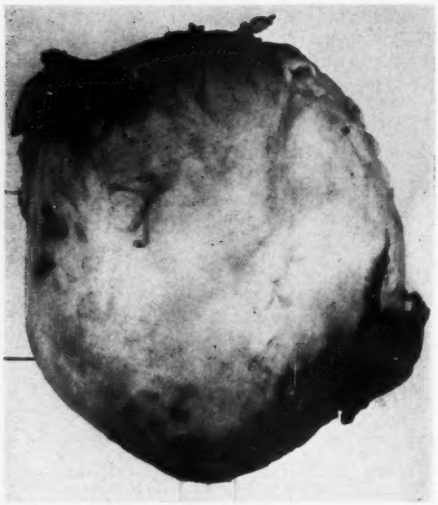


Fig. 4. Case 2: The tumor removed at operation was histologically a neurofibroma. The large size is characteristic of these neoplasms.

fibrous tissue stroma. On cross-section many of the fibers seem vacuolated and are considered to be of nerve origin. No ganglion cells are observed. No very cellular areas are present which could be interpreted as definitely malignant. *Diagnosis:* Neurofibroma, posterior chest wall.

The patient made an uneventful recovery and was discharged from the hospital on Nov. 11. He has returned from time to time for observation. He has been perfectly well and has no complaints. The most recent roentgen examination, March 2, 1939, was reported as follows: Residual fibrotic changes involving the right lung and pleura and deformity of the chest wall following removal of a large neurofibroma.

Comment: This case is an excellent example of the good results that may be expected from surgery in the benign neurogenic tumors of the chest, in spite of their very large size.

CASE 3: *Benign Lesion.* J. T. S., white male, age 54, was admitted to the Jefferson Hospital Sept. 23, 1940. His chief complaint was loss of weight and occasional wheezing.

The present illness began one year before, when the patient stated he started to lose weight and to experience swelling of his ankles, particularly during warm weather. This persisted and was accompanied by wheezing but absolutely no cough, pain, or dyspnea. His physician was suspicious of new growth and had a roentgen examination made of the chest. This revealed evidence of disease and the patient was referred to the Jefferson Hospital.

Physical examination was negative with the exception of the chest, which showed a marked limitation of expansion on the entire right side. There was absence of tactile fremitus, vocal fremitus, and breath sounds, with flatness over the right side posteriorly from the 7th rib down and from the vertebral column to the axillary line. Bronchovesicular breath sounds were present above the 7th rib. There was some clubbing of the fingers. The blood showed a slight anemia, the urinalyses were negative, and the Wassermann and Kahn reactions were negative.

Roentgen examination of the chest done by Dr. John T. Farrell, Jr., prior to admission, showed a large tumor occupying the lateral and posterior aspect of the base of the right lung. Its upper border was rather sharply circumscribed while its base was obscured by an effusion. The tumor was suspected of being a primary pulmonary carcinoma, although a benign lesion could not be excluded.

The *bronchoscopic findings* were meager. There was some compression of the external subdivisions of the right lower lobe bronchus but this was not marked.

Dr. Bradshaw was asked to see the patient and he reported as follows: There is a large intrathoracic tumor which I believe arises from the chest wall rather than the lung proper, probably one of the neurogenic tumors. However, there is enough suspicion that this tumor may be subdiaphragmatic to make me want to do a diagnostic pneumothorax. The pneumothorax will also prepare the patient for operation should he decide to go through with it.

The diagnostic pneumothorax was done and roentgenograms showed the tumor to better advantage.

At *operation* the 7th rib was removed in the postero-lateral line; a large, well rounded, smooth tumor, approximately 6 inches in diameter, was found between the right lower lobe and diaphragm. There were dense adhesions between the diaphragm and the tumor; these were separated and the diaphragm was perforated and then sutured with interrupted catgut sutures. There were only a few filmy adhesions between the tumor and chest wall. The right lower lobe was densely adherent to the tumor and a tourniquet was slipped above the tumor, which included part of the lower lobe, and this portion of the lobe (with the tumor) was removed. Raw surfaces of the right lower lobe were then inverted with fine chromic catgut, and intercostal tube drainage instituted below the incision.

The pathologic diagnosis was "neurofibroma."

In addition to the usual postoperative hydropneumothorax, there was a productive cough with considerable sputum. For this reason pneumonography was done, showing some enlargement and clubbing of the bronchi in the lower portion of the right lung. The patient was discharged from the hospital to the care of his family physician on Nov. 9, 1940.

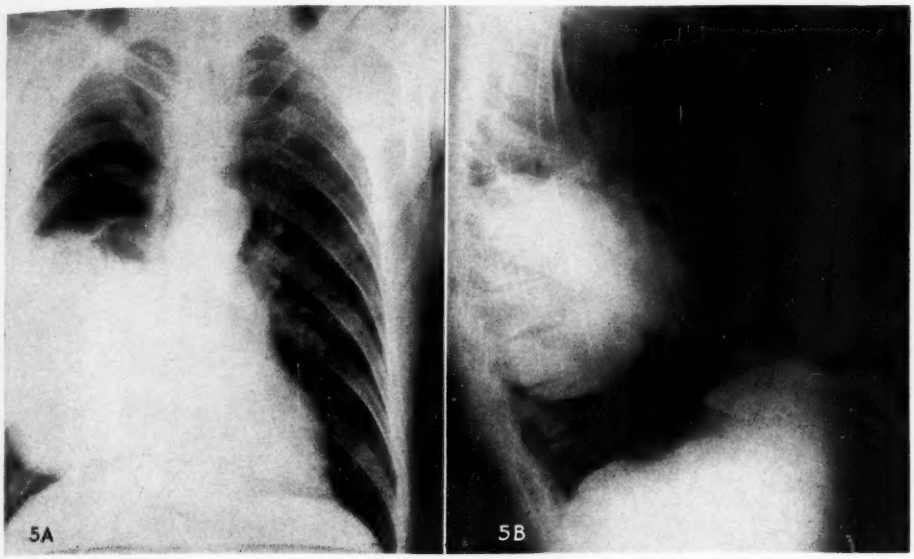


Fig. 5. Case 4: A. Neurogenic tumor of the right chest showing the large size attained by these neoplasms. B. Characteristic posterior position in the lateral view.

Comment: It appeared at the time of operation that this tumor had its origin from the diaphragm. Apparently these neurogenic tumors may arise from any structure within the chest.

CASE 4: *A Malignant Variety.* W. B., white male, age 55, was admitted to Jefferson Hospital March 9, 1937. His chief complaints were cough with expectoration of mucopurulent material for seven months, pain in the right chest, weight loss of 20 lb., and fever. A diagnosis of tuberculosis had been made, but sputum examinations were all negative and the patient was referred to Jefferson Hospital for bronchoscopy.

Physical examination showed no dyspnea or cyanosis. All signs were diminished both anteriorly and posteriorly from the 6th rib to the base of the lung on the right side. Fever was intermittent in type, averaging 101° F. The blood count showed a secondary anemia and 15,000 leukocytes. Sputum examinations were essentially negative. The Wassermann and Kahn reactions were negative.

Roentgen examination of the chest on March 11, 1937 (Fig. 5), was reported as follows: There is a large, sharply circumscribed mass in the lower medial and posterior aspects of the right lung. I believe it is a cyst and that it is exerting pressure on the upper lobe bronchus. There is no evidence of normal parenchymal markings over the upper lobe. This area has the appearance of a pneumothorax, though I suspect it is due to a large emphysematous cyst of the upper lobe.

The *bronchoscopic report* was as follows: Compression stenosis with forward displacement of right bronchus, the result of an extrabronchial lesion which could involve the lower lobe.

The patient stated that he had had clay-colored stools and hematuria and for this reason investigations of the gastro-intestinal tract and urinary tract were made, with negative results.

An *aspiration biopsy* of the tumor of the chest was done. A histologic study of the material obtained showed the lesion to be a malignant neoplasm, but it could not be further classified.

The patient's condition became progressively worse; there was a septic type of temperature, with a slight leukocytosis. A moderately severe secondary anemia was present, requiring repeated blood transfusions. A bronchopneumonia developed and death ensued just a month after admission.

At *autopsy* a large emphysematous cyst was found in the right lung, replacing approximately one-third of the upper lobe. The mid portion of the lung was replaced by a large, rounded tumor which was densely adherent to the posterior chest wall over a large area. The mass measured 12 × 16 cm., was soft and necrotic; on section the margins were sharply defined. It was composed of soft, yellowish-gray tissue, which was largely necrotic. It involved the lung merely by becoming adherent and not by actual infiltration. The large bronchi were compressed by the growth. The mediastinal and tracheobronchial lymph nodes were not involved. The pathologic diagnosis was malignant ganglioneuroma.

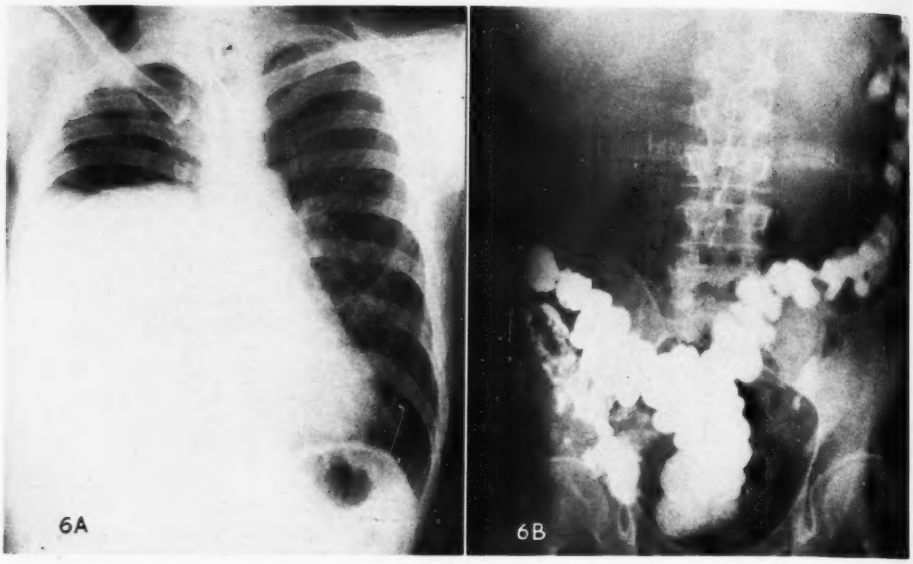


Fig. 6. Case 5: A. Immense tumor nearly filling the right chest. B. Palpable mass in the right upper abdomen and marked downward displacement of the colon, raising the question as to whether the tumor was in the chest or abdomen.

Comment: The marked loss of weight and rapid clinical course are quite characteristic of malignant lesions of the chest.

CASE 5: *An Ill-Advised Procedure.* M. L., white male, age 59, was admitted to the Jefferson Hospital on Oct. 11, 1939, complaining of pain in the lower right back since February 1939.

His *present illness* began with a cough due to a cold in November 1938. The cold disappeared but the cough continued, with expectoration of phlegm, with no blood and no odor. The patient began losing weight in February 1939 (18 lb.) and also suffered from soreness and ache in the lower right back. There was shortness of breath especially on exertion.

The patient was quite thin and poorly nourished. Expansion was decreased over the right side of the chest, where there was also dullness to percussion, except at the apex, with breath sounds poorly heard or absent. A large mass was palpable in the right upper abdomen. Its nature could not be determined. The blood and urine examinations and the Wassermann and Kahn reactions were negative.

Roentgen examination of the chest and abdomen on Oct. 11, 1939 (Fig. 6), was reported as follows: Examination of the chest shows a large, globular, very dense homogeneous shadow involving the lower two-thirds of the right hemithorax. The heart is slightly displaced to the left. There is considerable displacement of the esophagus to the left. The right border of the heart and the right dome of the diaphragm are obscured by the shadow. The upper portion of the right lung and the entire left lung are negative. Films of the abdomen show a marked downward displacement of the right half of the colon by a large soft tissue mass in the upper abdomen. The question arises as to whether we are dealing with a primary intrathoracic or an abdominal tumor. I am of the opinion that the lesion is intrathoracic and that its weight is displacing the diaphragm downward and this in turn is pushing the liver and colon downward. The lesion would seem to be some form of benign tumor such as a lipoma or a neurofibroma.

Bronchoscopic examination showed displacement and deformity of trachea and right bronchus with compression stenosis of the right bronchus.

Because of the right upper abdominal mass the possibility of a renal or adrenal tumor was considered and a right retrograde pyelogram was advised. This revealed a moderate degree of downward displacement of the right kidney due to extrarenal pressure from above. The kidney pelvis was normal in size and contour.

The patient was presented at the Tumor Clinic and because of the condition of the abdomen, a peritoneoscopy was suggested. Dr. Bradshaw advised against this procedure as being too dangerous in the presence of the large intrathoracic tumor and the disturbed pressure relationships in the chest and abdomen. In spite of his advice, the peritoneoscopy was attempted. Approximately 50 c.c. of air had been injected when the patient lost consciousness, became cyanotic, and ceased to breathe. The peritoneal cavity was rapidly opened to a 4-inch

incision but little air escaped when the peritoneum was incised. The liver was found practically beneath the trocar. There was a small amount of blood present in the peritoneal cavity. Exploration was limited to palpation of the liver, which extended from the diaphragm to the pelvic brim on the right side. Although the heart continued to beat for two or three minutes, artificial respiration was instituted but the patient could not be resuscitated.

At *autopsy* the large tumor of the chest was found to weigh 3,750 gm. and to measure 10.5 × 6 × 9 cm. It had a definite capsule and the right lung was bound to it by numerous adhesions. The tumor was firm and a very pale yellow. On section it consisted of interlacing bundles and whorls of yellowish-gray tissue that protruded from its surface when the mass was cut. The histologic diagnosis was neurofibroma, atelectasis of the right lung, chronic passive congestion of the liver and spleen, and focal chronic nephritis.

Comment: This fatality shows that in the presence of these large tumors the patient's reserve can readily be upset. At autopsy, it was apparent that the tumor could have been easily removed and since it was benign the prognosis would have been good. This tumor was of immense size and serves well to illustrate the dimensions which these neurogenic tumors may attain before giving rise to symptoms.

CASE 6: *Spinal Cord Involvement.* D. R., white female, age 49, was first studied in the Out-Patient Department, Jefferson Hospital. In April 1939 she was complaining of soreness of the throat and difficulty in swallowing, of about two months' duration, more marked during the past four or five weeks. She stated that food seemed to lodge in the mid thoracic region, especially solids, and she had to force it down with liquids. There was loss of weight. A *roentgen examination* of the esophagus revealed a smooth narrowing at the level of the aortic knob but no definite evidence of an organic lesion. *Esophagoscopy* was negative.

On Aug. 2, 1940, the patient was admitted to the Jefferson Hospital complaining of pain in the back for three months, numbness of the legs for six weeks, and stiffness of legs for five weeks.

Her present illness began three months before admission, with pain in the back radiating down the spine and across the shoulders. She tried home remedies and then consulted a physician, who treated her for arthritis, with no benefit. She was sent to a hospital and while there experienced numbness in both legs and, shortly afterward, retention of urine and feces. In about a week she lost control of her legs and became "stiff" from just beneath the breasts down. She left the hospital and a few days later was admitted to Jefferson. Pain in the back was of a burning type and constant. There seemed to be a constriction just under her breasts.

Physical examination showed paralysis from the waist down. The patient was ill, febrile, and toxic. A complete neurologic examination led to the impression of a compressing extramedullary spinal cord lesion at about the level of the 4th to the 6th dorsal vertebra. Metastatic carcinoma, sarcoma, and multiple myeloma were suggested as diagnostic possibilities.

Spinal tap and a Queckenstedt test of the cerebrospinal fluid showed an initial pressure of 165 mm. There was no rise with right or left jugular or bilateral jugular compression. With abdominal compression the pressure rose to 295 mm. in ten seconds and fell promptly in ten seconds. Six cubic centimeters of clear xanthochromic (slightly yellow) fluid was removed; final pressure 100 mm.

A gynecologic examination revealed a pelvic tumor which was not considered malignant. (There was a history of uterine tumors discovered three years before.) On urologic examination the patient was found to have a cord bladder with acute urinary tract infection.

Roentgen examination of the chest and thoracic spine, Aug. 5, 1940 (Fig. 7), was reported as follows: There is evidence of a destructive process beginning to involve the body of the 5th thoracic vertebra, with a tendency to slight narrowing of the body, particularly the right lateral half, but there does not seem to be any disturbance in the intervertebral spaces. There is a large soft tissue mass at about the 5th dorsal vertebra, predominantly on the right side. The other thoracic vertebrae seem to have a normal appearance. The lungs are negative for any active pulmonary disease or metastatic lesion. The heart is normal in size and shape. The aortic shadow cannot be clearly made out because of the superimposed shadow of the soft tissue mass in this region, but I do not believe the changes represent an aneurysm. *Interpretation:* Destructive changes in the body of the 5th thoracic vertebra with surrounding soft tissue mass. Changes may be inflammatory or secondary to a neoplastic lesion.

Roentgen examination of the esophagus showed no evidence of an organic lesion, although there was a little tendency to spasm in the region of the mass noted on previous examination. There seemed to be a slight displacement of the esophagus in this region to the left.

Because of the intermittent fever and the roentgen findings, the possibility of a mediastinal abscess or osteomyelitis of the vertebrae was considered. An aspiration biopsy through the posterior chest wall was attempted but was unsuccessful.

On Aug. 12, the patient was *operated* upon through a posterior incision at the level of the 4th dorsal vertebra on the right side. About three inches of the 4th rib were removed and the tumor was located. A small piece was removed for a frozen section and the wound was closed. The histologic

report was malignant neurogenic tumor. In view of this report and the poor physical condition of the patient it was not thought advisable to resort to a laminectomy or other surgery. Death occurred Aug. 22.

Comment: This case is an example of the so-called "dumb-bell" type of neurogenic tumor, one portion of which is inside the vertebral canal, giving rise to spinal cord symptoms, while the other portion is outside the canal and may or may not give rise to symptoms. Such tumors are fairly common and roentgenologically often produce an enlargement of the intervertebral foramen at the site of involvement.

CASE 7: *Neurogenic Tumor of Unusual Origin.* H. E., white female, age 14, was admitted to Jefferson Hospital Nov. 1, 1939. Her chief complaint was difficulty in swallowing, beginning in March 1939 and gradually becoming more marked. She began vomiting in May and this had continued to date. There had been a 20-lb. weight loss since the onset of symptoms. The patient complained also of pain in the epigastrium and a sensation of fullness. She was first seen in the Out-Patient Department and was referred for a roentgen examination of the esophagus, which was done on Oct. 25 (Fig. 8). This showed the chest to be essentially negative except for a forward displacement of the trachea in the lateral view, such as is seen in dilatations of the esophagus. A marked obstruction of the esophagus was present several inches above the diaphragm, with compensatory dilatation proximal to the obstruction. Several diagnostic possibilities were suggested: achalasia, cicatricial contraction congenital stenosis.

While the roentgen appearance of the lesion resembled that of an achalasia, the point of obstruction was much too high. There was no history of any cause for a cicatricial contraction of the esophagus.

Physical examination on admission showed the patient to be thin and undernourished and somewhat sickly looking. The cervical lymph nodes were palpable. The heart, lungs, abdomen, and extremities were negative. The laboratory examinations, including Wassermann and Kahn reactions, were negative.

The esophagoscopic diagnosis was neoplasm of the lower end of the esophagus apparently arising posteriorly and producing marked stenosis. The origin and character of the growth could not be determined accurately. The growth appeared firm, its surface was definitely lobulated, but apparently not ulcerated. It did not exhibit any tendency to bleed when touched.

A gastrostomy was performed because of the inability of the patient to swallow a sufficient amount of food to maintain normal nutrition.

Esophagoscopy was repeated on several occasions and a retrograde esophagoscopy was also done. No involvement of the cardiac end of the stomach was found. Under observation, the tumor was apparently increasing in size. A biopsy was taken by means of the esophagoscope. The tissue obtained was diagnosed histologically as chronic inflammatory tissue, with no evidence of malignancy. A course of deep roentgen therapy produced no appreciable change in the appearance of the esophagus. In February 1940 a piece of tissue removed from the esophagus was strongly suggestive histologically of a neurofibroma.

The patient was discharged from the hospital on Feb. 8, and was readmitted several times. Repeated studies showed little change from previous investigations. The general condition remained about the same but in May pain in the epigastrium and upper lumbar spine developed, for which no adequate cause could be found.

The patient's final admission was on Oct. 13, 1940, at which time Dr. Bradshaw advised an exploratory thoracotomy.

At *operation*, Oct. 25, an incision was made over the 9th rib, left side. This rib was removed with the posterior portion of the 8th rib. The pleura was incised and a very hard, nodular mass measuring about 8 cm. in greatest dimension was found wedged between the aorta, esophagus, and lung. The lesion was only about 3 cm. from the diaphragm at its distal end. It invaded the contiguous lung and esophagus, which had to be cut away with the growth. The proximal and distal ends of the esophagus were ligated. The right mediastinum was punctured during the procedure but no respiratory distress resulted. The chest was closed. Incision along the left side of the neck was made. The esophagus was dissected free and pulled up and then transplanted under the skin at the angle of Louis. The patient died on Oct. 28. Autopsy was refused.

The operative specimen consists of a tubular tumor taken from the esophagus, measuring 7 × 4 cm. Most of it appears to be fairly well encapsulated. The mass is firm in consistency and diffusely grayish-white in color. In the center of one end is apparently the remnant of the esophagus. The mucosa is rough and somewhat polypoid. Histologic sections are made up largely of fibrous tissue which has a whorl-like arrangement. Throughout there is considerable inflammatory change. In some areas the tumor is quite cellular. The histologic picture conforms to that previously described. The tumor appears to be a benign one arising from the coverings of nervous tissue, and must be placed in the group of *neurofibromas.*

Comment: This case is quite distinct from the others and its true nature was not suspected either clinically or roentgenologically. It illustrates well the varied origin of these neurogenic tumors.

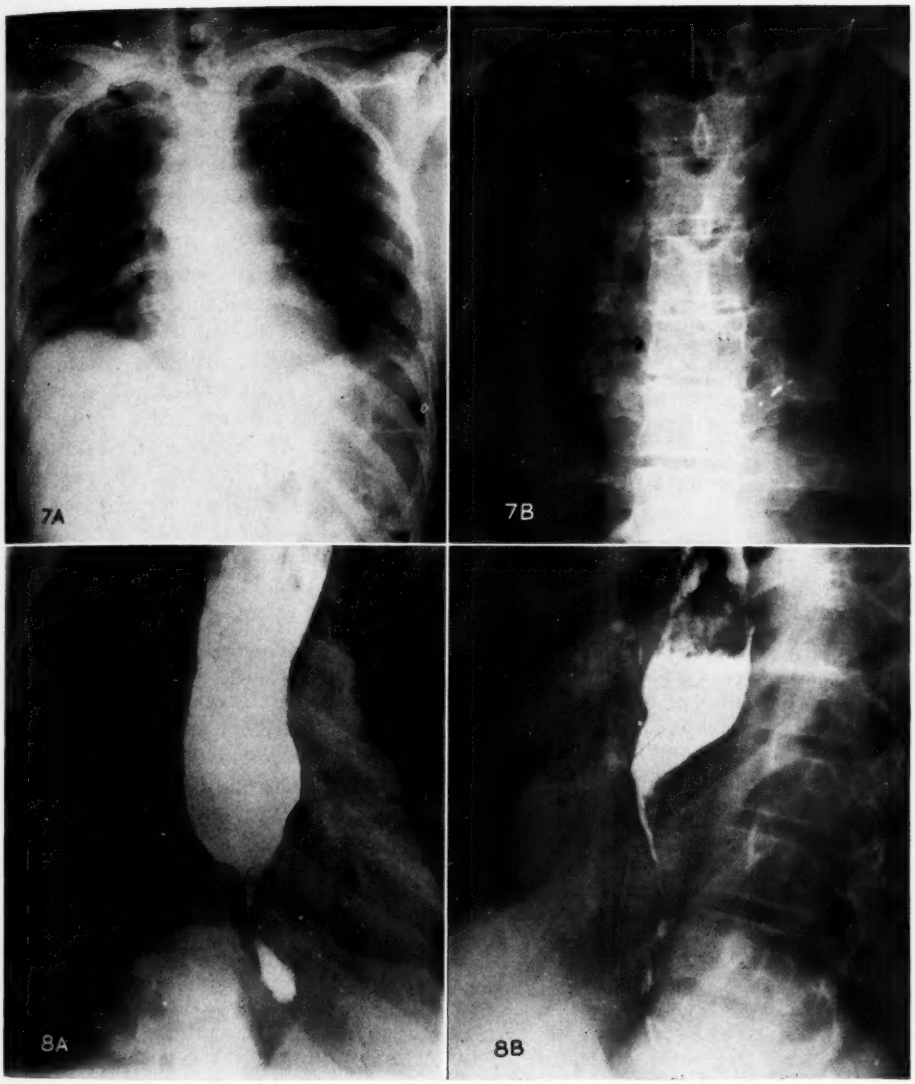


Fig. 7. Case 6: A. Neurogenic tumor in the posterior mediastinum, indicated by the arrows. B. Bucky film showing erosion of the 5th dorsal vertebra by the tumor. The lesion had invaded the vertebral canal, giving rise to spinal cord symptoms. This is an example of the so-called "dumb-bell" type of neurogenic tumor.

Fig. 8. Case 7: This neurogenic tumor had its origin in the wall of the esophagus, causing almost complete obstruction. This is an unusual site but apparently these neoplasms may arise from any structure within the chest.

CASE 8: *An Error in Diagnosis.* M. S., white male, age 19. In the fall of 1938, Dr. William C. Troxell, of Allentown, Pa., brought to one of us (K. K.) a single postero-anterior film of the chest of this patient (Fig. 9) for an opinion. The tumor in the right chest had the typical appearance of a neurofibroma and this diagnosis was suggested. Dr. Bradshaw was asked to see the film and concurred in the diagnosis. The patient was admitted to Jefferson Hospital Nov. 12, 1938. His chief complaint was of a cough of four months' duration and hemoptysis for three months. He tired easily and there had been a loss of weight of 20 lb. during the past year.

The present illness began about four months before admission, with a dry cough. A month later the

patient began to cough up sputum tinged with red. His family physician sent him to the Allentown Hospital, where a roentgen examination was made of the chest and a series of x-ray treatments were administered by Dr. Troxell. A second series of treatments followed three weeks after the completion of the first. There was no apparent change in the tumor as the result of therapy.

Physical examination showed diminished expansion of the right side of the chest; percussion note dull over the middle and lower part of the right side posteriorly; breath sounds decreased and vocal fremitus and resonance increased over the same area. Laboratory studies were negative.

Roentgen examination of the chest (Fig. 10) was reported as follows: There is a sharply circumscribed rounded shadow over the lower part of the right chest in the anteroposterior view, and in the anterior third in the lateral view. It appears to correspond to the location of the right middle lobe. The pleura is thickened around both sides of the shadow and there appears to be a small adhesion running from its lower portion to the diaphragm. The other portions of the lungs are well aerated. The right half of the diaphragm is a little elevated and does not move as freely as the left side. There is no apparent displacement of the heart. *Interpretation:* Sharply demarcated rounded mass in region of right middle lobe which might be the result of an infected cyst or a peculiar interlobar effusion.

Because of the anterior position of the tumor as seen in the lateral view, it was felt rather definitely that this was not a neurofibroma as originally diagnosed from the postero-anterior film alone. Operation, however, had already been begun.

An antero-lateral incision was made along the rib, which was resected (right side). On entering the pleural cavity a large tumor the size of a grapefruit was discovered, occupying the greater part of the middle lobe and extending into the upper and lower lobes. A biopsy was taken and the frozen section report was adenocarcinoma. A right pneumonectomy was performed.

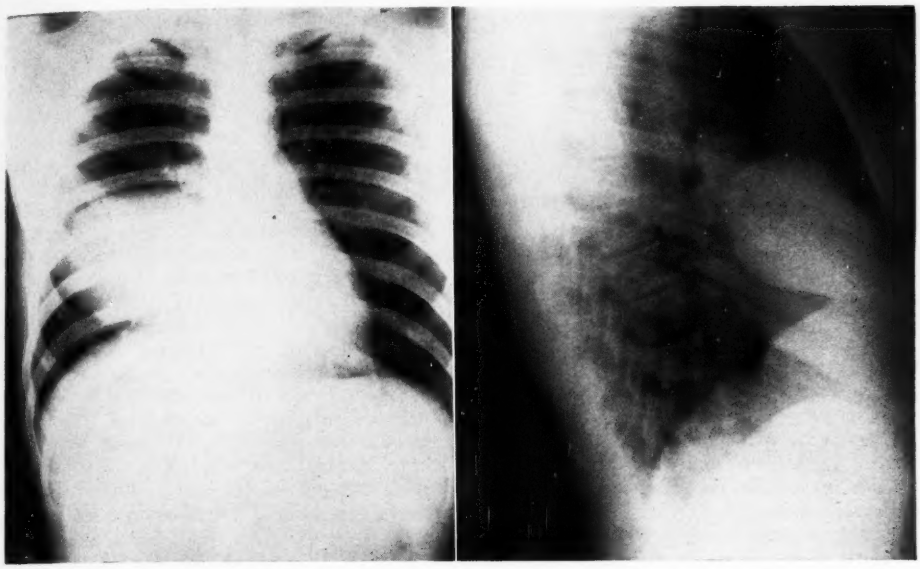
The postoperative course was quite satisfactory. A more thorough examination of the lung tumor showed that histologically it resembled an embryonal carcinoma. On questioning the patient, it was found that he had had a mass in the right scrotum for three years, which was slowly increasing in size. On examination the right scrotum was found to be three to four times the normal size. Palpation revealed a hard, smooth, globular swelling. The testis and epididymis could not be definitely differentiated. A teratoma of the testis was suspected. A right orchidectomy was performed on Dec. 9, 1938, and the diagnosis of embryonal carcinoma of the testis was made histologically.

The patient was given a series of deep roentgen therapy over the pelvis, abdomen, and chest, but evidence of recurrence developed in the right chest and he died on April 13.

Comment: A number of rather obvious errors were made in the management of this case. The operation should not have been undertaken without a lateral roentgenogram of the chest. The anterior position of the tumor was strong evidence against a neurofibroma. This emphasizes the necessity of a thorough and adequate roentgen examination before therapy is considered. The loss of weight should also have suggested the probable malignant nature of the lesion. And obviously, the physical examination could not have been very thorough since the tumor of the testicle was not discovered until after the operation. While fortunately these errors did not alter the outcome, this experience nevertheless emphasizes the fact that no matter how obvious a case may appear, it still warrants the most careful and painstaking consideration.

DISCUSSION

The occurrence of seven intrathoracic tumors during the past four years would indicate that these neoplasms are not as rare as they are generally regarded. More pertinent is the fact that in only one of the seven was the correct diagnosis made roentgenologically. Yet in the typical case the roentgen manifestations are so characteristic that the lesion should be recognized in the majority of instances. A dense, rounded, well circumscribed shadow in the posterior portion of the chest, and of considerable size, should suggest the presence of a neurogenic tumor. The existence of a mass in the posterior mediastinum associated with spinal cord symptoms is most likely to be a neurogenic tumor. Whether such a tumor is benign or malignant cannot usually be determined roentgenologically. The true nature of these tumors can seldom be suspected when they arise from unusual sites, as for example the esophagus (Case 7). One of the two cases diagnosed roentgenologically as a neurofibroma proved to be a metastatic lesion (Case 8). This error was due to the fact that a lateral view of the chest was not at hand. These cases illustrate the neces-



Figs. 9 and 10. Case 8: A diagnosis of neurofibroma was made from the postero-anterior film (left). The lateral view (right), made the day of operation, shows the anterior position of the lesion, which is very much against the diagnosis of a neurogenic tumor. The final diagnosis was metastatic carcinoma secondary to an embryonal carcinoma of the testis. This case emphasizes the importance of the lateral roentgenogram.

sity of a careful and adequate roentgen study, which is by far the most important single examination in the detection and recognition of intrathoracic neurogenic tumors.

The clinical manifestations of these neoplasms are by no means characteristic and are of little help in the diagnosis. They are limited to pressure phenomena and vary with the structures pressed upon. A fairly rapid course, and particularly a marked loss of weight, suggest the malignant nature of the lesion. Helpful in the clinical investigation are diagnostic pneumothorax, bronchoscopy, and aspiration or punch biopsy. Surgical exploration for diagnostic purposes should be done when necessary. Surgery is the treatment of choice. When the lesion is benign, which is usually the case, the tumor can in most instances be quite readily removed. Since neurogenic tumors are highly radioresistant, irradiation is of no value in treatment. Generally speaking, the prognosis following surgical removal is very good in the benign tumors. As usual, the earlier the diagnosis and treatment, the more favorable the outlook.

SUMMARY

1. Attention is directed to the frequency, variability, and recognition of intrathoracic neurogenic tumors.

2. Seven such neoplasms and one metastatic lesion simulating a neurogenic tumor are reported.

3. The clinical manifestations are detailed and the means of diagnosis are discussed.

4. The importance of the roentgen examination is emphasized and the roentgen characteristics of intrathoracic neurogenic tumors are described.

1020 Sansom St., Philadelphia, Penna.

REFERENCES

1. ANDRUS, W. D., AND HEUER, G. J.: Surgical Treatment of Tumors of the Mediastinum. Surg., Gynec. & Obst. **63:** 469–482, October 1936.

2. BIGLER, J. A., AND HOYNE, A.: Ganglioneuroma: Report of Two Cases with Review of the Literature. Am. J. Dis. Child. **43:** 1552–1571, June 1932.

3. BOHRER, J. V., AND LINCOLN, E. M.: Ganglioneuroma of the Chest in Children. J. Thoracic Surg. **3:** 365–373, April 1934.

4. HARRINGTON, S. W.: Diagnosis and Treatment of Anterior and Posterior Mediastinal Tumors. New York State J. Med. **35:** 1073–1080, Nov. 1, 1935.

5. HARTUNG, A., AND RUBERT, S. R.: Roentgen Aspects of Sympathetic Neuroblastoma. Radiology **24:** 607–615, May 1935.

6. LEWIS, D., AND GESCHICKTER, C. F.: Tumors of the Sympathetic Nervous System. Arch. Surg. **28:** 16–58, January 1934.

7. MCFARLAND, J.: Ganglioneuroma of Retroperitoneal Origin. Arch. Path. **11:** 118–124, January 1931.

8. RIGGS, T. F., AND GOOD, L. P.: Ganglioneuroma of Mediastinum Requiring Surgical Intervention for Relief of Obstructive Symptoms. Arch. Surg. **19:** 309–320, August 1929.

9. WAHL, H. R.: Neuroblastomata: with a Study of a Case Illustrating the Three Types That Arise from the Sympathetic System. J. M. Research, **30:** 205–260, 1914.

DISCUSSION

LeRoy Sante, M.D., (St. Louis, Mo.): The essayist has covered his subject in his characteristically thorough manner, leaving me little to do but emphasize some of the things he has said.

From a practical standpoint in the diagnosis of neoplasms of the thorax, the radiologist is first of all confronted by the question as to whether or not the lesion seen in the chest is of neoplastic or inflammatory origin. If, after correlation of the clinical and radiologic findings, the probability of neoplastic disease is established, the principal factors for consideration become: whether the tumor in question is benign or malignant, and, if malignant, whether it is primary or metastatic.

Elsewhere in the body we ordinarily think of one of the characteristics of a benign tumor as its sharply outlined encapsulated border, but this cannot be relied upon as a criterion of benign character in chest tumors. In this location most malignant tumors present just such a rounded nodular appearance. The relatively limited types and infrequent occurrence of benign tumors of the lung, however, render the predominating likelihood in favor of malignancy.

The problem then becomes one of determination of the primary or metastatic character of the growth. Since the lungs are so favorably situated for and are so commonly the site of metastatic malignant neoplasms, the burden of proof under such conditions would seem to be in favor of secondary malignant lesions. However, if a thorough search of all other locations fails to reveal any evidence of a primary growth, then it must be assumed that the tumor in question is primary in character.

You will perceive by this system of reasoning how much, in the ultimate diagnosis of malignant lesions of the chest, depends upon statistical probabilities and how much depends upon exercise of judgment.

Now it is true that certain types of tumor have certain predominant characteristics of growth and location. For instance, it is generally accepted, I think, that neurofibromata usually occur in the posterior portion of the chest, whereas dermoids are most frequently encountered in the anterior portion; that lymphoblastomas most frequently occur in the mediastinum and mid portion of the lung and bronchiogenic carcinomata occur around the hilum region and central portion.

Furthermore, it is true that some tumors have certain characteristics which aid in their specific identification as, for instance, the straight line fluid level seen in dermoids, in the upright position, due to the supernatant oily substance contained in the cyst.

By judicious care in correlating the clinical with the roentgen findings, it should be possible, therefore, to come to a correct conclusion not only as to the malignant or benign character of a growth, but even to speculate as to the nature of the cell structure.

The pathologist may be faced by a dilemma in determining the malignant character of a growth even with the section under the microscope; it is frequently possible for the radiologist to come to a more exact opinion. This is especially true of fibrous tissue tumors such as neurofibromata and fibrosarcoma.

As an illustration, may I cite two cases. Both of these patients had multiple fibrous tissue tumors of the skin all over the body. Microscopic examination led to a diagnosis of benign neurofibroma and yet in both instances large metastatic lesions appeared in the lungs and in one case practically all of the organs of the body were involved, including heart, lungs, liver, and other abdominal organs.

One may predict, therefore, in many instances, the type of tumor from the roentgen evidence with as fair a degree of accuracy as the pathologist, but it is always wise in making predictions to do so with proper reservations.

Silicosis[1]

GAGE CLEMENT, M.D.
Duluth, Minnesota

IN THIS DISCUSSION on silicosis it should be clearly understood that the opinions expressed are the result of personal observations in the mining industries in the north central part of the United States over a period of about ten years. It has not been found possible to apply all the information obtained from various articles and discussions on silicosis to conditions existing in the area with which I am familiar.

Most articles on silicosis, for example, assume, without the consideration of a doubt, that all rock drillers in underground mines have silicosis. This is not true. In one mine with which I am acquainted no silicosis is evident in any of the workmen. This is due to three things: (1) water seeps through the walls of the mine, which are constantly wet; (2) the rock and "dirt" contain less than 12 per cent silica, the average run being 7 per cent; (3) the ventilating system of the mine is practically ideal. In another mine, however, less than one mile away, silicosis does exist. But in this mine the rock contains 65 to 72 per cent silica, the walls are not wet, and the ventilation is not very good.

Another common assumption is that an atmosphere laden with silica dust predisposes to tuberculosis and that most silicotics eventually have tuberculosis. In one group of three mines with which I am acquainted, not only is the percentage of pulmonary tuberculosis less in the silicotics than in the other inhabitants in the surrounding country, but the incidence of "head colds" and pneumonia is lower. Also the morbidity and the mortality from pneumonia in this particular group of silicotics are less than in the general population in the same locality.

It should also be understood that silicosis is not a disease, that it is not disabling, and that it is not a cause of death. Simple silicosis does not directly participate in the production of any disease and it does not increase the incidence of any disease. Only in its advanced stage and when it is accompanied by the infirmities of age does it show any tendency to limit one's activities. These conclusions, also, are the result of personal observation. This observation consists not only of looking at chest films, but of studying the conditions under which the miners work, participating in some of the physical examinations which are conducted regularly, assisting in taking the industrial histories and in follow-up investigations, and consultations with the personal physicians of the miners and their families, physicians who are not associated in any way with the mining industries. With such opportunities, it is possible to consider the silicosis problem from the point of view of both the employer and the employee and to form a practically unbiased opinion.

From year to year State Industrial Commissions in the United States have taken more and more interest in silicosis. In several states, the legislatures have passed laws defining silicosis and limiting or regulating the compensation permissible therefor. In some of the states, in which the statutes have not covered the condition, trial by jury is the only method of determining the amount of disability to which the plaintiff is entitled. In most of the many trials to which I have been called as an expert witness, there has been such a diversity of opinion as to what constitutes silicosis and what constitutes disability that not only has the jury been confounded but counsel and court also.

This diversity of opinion on the part of medical witnesses is probably the result of the following factors: (1) an inadequate understanding of what simple silicosis

[1] Read before the Radiological Society of North America at the Twenty-sixth Annual Meeting, Cleveland, Ohio, Dec. 2–6, 1940.

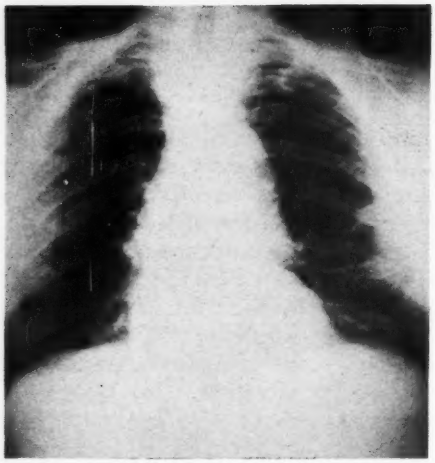


Fig. 1. Simple silicosis: prenodular stage.

really is; (2) an inadequate understanding of the influence of infection on silicosis; (3) failure to realize that simple silicosis is not a disabling condition; (4) a definite sympathy on the part of the witness for the plaintiff without due consideration of the cause of the disability, if one exists; (5) failure to realize that the incidence of infection is no greater in silicotics than in others; (6) lack of realization that more than 90 per cent of silicotics are at work in the occupation in which the silicosis was acquired; (7) failure to realize that simple silicosis is rarely seen in the hospital or clinic; (8) failure of the witnessing physician to know silicosis as a result of participating in one or more silicotic survey in an industry in which the condition really exists; (9) lack of knowledge of the size, number, and silicon percentage of the dust particles inhaled, together with the length of exposure, in the particular industry from which the workman comes; (10) a woeful lack of knowledge of what a chest film of simple silicosis looks like. A few remarks under some of these headings may not be amiss.

An inadequate understanding of what simple silicosis really is results from lack of conscientious study of the condition. Many of the articles appearing in the literature follow the lead of some of the early original papers on the subject, clearly manifest no attempt at originality, and show a decided disinclination to stray from the opinions of others.

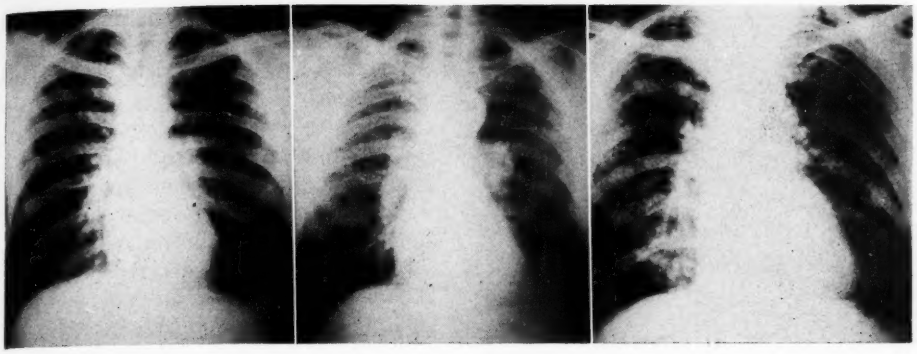
Too much has been written upon the influence of infection on silicosis and these contributions also show a lack of investigation on the part of the authors. Too many reports have been made of only one or two cases, with one or two illustrations showing the particular patients. These reports leave the impression that, because the cases presented were of a given character, all cases are therefore similar.

The failure of the physician to realize that simple silicosis is not a disabling condition is dependent upon the fact that he has never participated in a survey of silicosis and has never seen hundreds of men who are perfectly healthy though having an extensive amount of silicotic nodulation over both lung fields.

Sympathy for the plaintiff without determining the cause of his disability is common. This is illustrated by a suit brought in Minnesota in which one physician testified that the patient's disability was due solely to silicosis. As a matter of record he overlooked the fact that the plaintiff had active pulmonary tuberculosis, intestinal tuberculosis, syphilis with bulbar palsy, and extensive hemorrhoids. The chagrin of this witness when he heard the testimony of a disinterested physician can be imagined.

Perhaps the greatest fault of witnessing physicians is attributable to the fact that simple silicosis is rarely if ever seen in the clinic or hospital. Yet many physicians are firmly of the opinion that the silicotic with infection whom they see in the hospital or office presents a true picture of simple silicosis. Being a non-disabling condition, silicosis does not require the attention of a physician.

Some physicians fail to apply their knowledge of the size, number, and silicon percentage of the dust particles required to produce silicosis over a given length of time. They are too inclined to take the word of the plaintiff himself, or his attorney



Figs. 2–4. Simple silicosis: from left to right, first, second, and third stage nodulation, with nodules about 2 mm., 4 mm., and 6 mm. in diameter, respectively.

or an associated workman, for facts relative to the dusty occupation. In a recent action at law, it was the testimony of three workmen that the place of occupation at the breast in a mine was dusty and that on account of the dust present the visibility was very poor. The testimony was so convincing that the attorneys and physicians for the plaintiff felt sure that dust alone was responsible for the poor visibility. On impartial investigation, however, it was found to be due entirely to moisture in the atmosphere, produced by the air pressure and by the water in the water-liner used at the job.

The length of time in years, months, and days, of exposure to dust must also be taken into consideration. In another action at law in which I had been called as a witness for the plaintiff, the suit was withdrawn because, in going over the exhibits, I discovered, from the time-sheets which the plaintiff himself had submitted in evidence, that his period of work for the defendant company was only two years, three months, and twenty days out of a total working period of nineteen years.

The tenth factor I mentioned as accounting for the diversity of opinion among medical witnesses is the woeful lack of knowledge of what a film of simple silicosis looks like. This is not all the fault of the physician who testifies but is partly the fault of the writers on the subject. For example, out of eleven publications on the subject of silicosis, two had fifteen illustrations each of chests, with only one illustration in each showing silicosis. Another had two reproductions of chest roentgenograms, neither of which showed silicosis. Still another had seventeen illustrations, of which only one was silicosis. Three others with seven, eight, and eleven illustrations, had one each of silicosis, and four articles had four, five, seven, and eight illustrations respectively with none of silicosis. Evidently a knowledge of what a chest roentgenogram showing only simple silicosis looks like cannot be obtained from the literature.

These observations have led to the presentation of this paper and of some roentgenograms of simple silicosis as it exists in men who are not disabled, who are still employed in the occupation in which the condition was acquired. It is possible to reproduce but a few from many hundreds of films of men who go on day after day in their usual occupation, without any sign or symptom of disease, content in their employment and able to do a full day's work. One of these reproductions (Fig. 5) shows the chest of a man fifty-five years of age who has worked as a rock-driller and shift-boss for almost thirty years in the same mine. He is known to me personally and I have assisted in his physical examination a number of times. His only physical complaint is that he some-

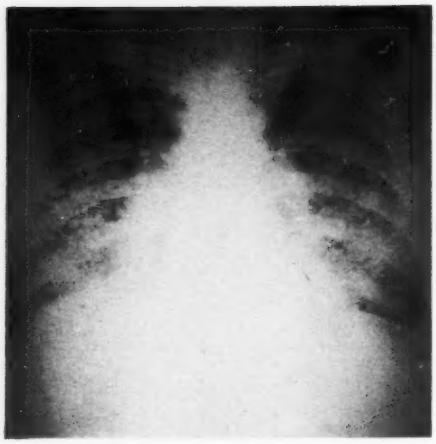


Fig. 5. Simple silicosis: third stage nodulation, in a "shift-boss," fifty-five years of age. No disability.

times gets a little short of breath when he runs up a thirty-foot ladder from one mine level to another. At fifty-five he is becoming a little corpulent but physical examination shows that he is perfectly normal.

The various classifications of the different stages or degrees of silicosis are familiar to all of us. We assume that such classifications are necessary, but when it is practically impossible to sort or allocate our roentgenograms into these various groups and to state without hesitation that one workman has second stage silicosis and that another has third stage silicosis, then the classifications are of little practical value. I have never seen a film of the so-called anteprimary or prenodular stage of silicosis in which I could not, by careful examination, find some evidence of nodulation. Yet the anteprimary stage is supposed to be a prenodulation stage. One is taking a risk in making a definite diagnosis of prenodular silicosis without knowing the conditions under which the man works, the characteristics of the silica dust to which he is exposed, and the length of the exposure. After nodulation is well established the diagnosis is more self-evident.

No new or different classification will be presented today. There probably is a prenodular stage. After nodulation becomes apparent most examiners who see many films of silicosis think in terms of three stages. These are not differentiated on the basis of the number of nodules but of their size. The first stage is that in which the nodules measure about 2 mm. in diameter; the second stage that in which the nodules measure about 4 mm. in diameter, and the third stage that in which the nodules measure about 6 mm. A careful check of serial roentgenograms, made over a period of several years, leads us to believe that the nodules rarely increase in number, but merely in size. Large, massive or conglomerate areas, "pop-corn balls," "pawn-brokers' signs," linear or plane fibrosis, thickening of the pleura, tenting of the diaphragm, cavitation, and any involvement of the apices above the first rib or the lower outer margins of the lungs which occupy the costophrenic sulci indicate infection. This is not always tuberculosis. In fact, tuberculous infection is no more frequently seen in comparison with other infections than in the non-silicotic contiguous population. The old idea of "miner's consumption" is a hand-me-down from one authority to another, until the average physician has forgotten, as far as miners are concerned, that tuberculosis is caused by the Koch bacillus and not by silica dust.

What then is the roentgen picture of simple silicosis? In the prenodular stage, that stage which is ordinarily classified as the first stage, the appearance is that of enlarged hila with a relative increase in the density of the hilar shadows and an increase in the density and size of the truncal and linear markings. These markings do not extend farther into the outer lung field than do normal linear markings. Nowhere do these lines touch the periphery. There is no parenchymal involvement. Occasionally a faint generalized haziness is present. In this stage, also, small discrete spots measuring a millimeter or less in diameter are often apparent. They appear close to the hila and to the linear markings. These spots are the earliest visible evidence of nodulation.

The stage of nodulation changes the picture in that, as nodulation develops, either there is some emphysema present or the nodulation appears to overshadow the linear increase; in the well developed nodular stage there seem to be less hilar enlargement and less increase in the linear markings than were seen in the first stage. The nodulation makes its first appearance in the central zone of the lung fields, usually a little more marked on the right side than on the left. As time goes on the nodules increase in size, but not in number, so that in later years they appear to occupy more and more space in the lungs. This evidence of development is probably actual, yet with the increase in size there is no increase in number. The apices of the lungs never become involved. The costophrenic angles are also clear. No change in the size or shape of the heart occurs in any stage of simple silicosis, and the diaphragm and blood vessels remain normal in appearance. Any deviation from normal in the appearance of the organs inside the thoracic cage, except the discrete nodulation, is *prima-facie* evidence of disease or abnormality and is in no way associated with simple silicosis.

An attempt has been made to show that simple silicosis is not a disease, that it is not disabling, and that it is not a cause of death. Any abnormality inside the thoracic cage, aside from simple discrete nodulation, is not silicosis.

915 East First Street, Duluth, Minn.

DISCUSSION

Leo G. Rigler, M.D. (Minneapolis, Minn.): I am sure that all of us would agree with many of the things that Dr. Clement has said. Certainly there is no doubt that the index of the degree of disability is not the extent of the findings in the roentgenogram. On the other hand, I think Dr. Clement made the statement that simple silicosis is not disabling or the cause of death. There is no justification for such a statement if it is meant to apply to all silicotics.

I have seen three autopsies in the last three years in patients who, so far as we could determine on pathological examination, had nothing but silicosis and who died from that condition—I'd prefer to call it a disease. In one of these cases there was right heart failure. It might be objected that this case was not one of uncomplicated silicosis but the heart failure was a direct and unequivocal result of fibrosis of the lungs. In the other two there was right heart enlargement and the patients died of exhaustion because the lung was so fibrotic that their vital capacity was reduced below a point compatible with life.

I should like to ask what constitutes simple silicosis. We hear a good deal about the effects of infection, but which one of us has not had a respiratory infection at various times in his life. It is possible that among certain groups of miners the incidence of infection may be low, and it is very possible that in that group, because the incidence of infection is low, the incidence of disability is also low.

On the other hand, we must avoid the danger of saying that those persons with silicosis who are not disabled have simple silicosis while those who are disabled must have had an infection. The distinction, so far as I can tell, is not a very sharp one, without autopsy studies. Even then there is certainly a question as to whether it can be demonstrated unequivocally that some infection was not present at one time or another. I am not talking of tuberculosis, but any other type of infection such as Dr. Clement mentioned. I do not think there is much doubt in the minds of most of us that infection modifies the course of silicosis appreciably.

With regard to another point—that simple silicosis does not predispose to any disease—this may be true among the miners in Northern Minnesota; it certainly has not been my observation, though I have not had Dr. Clement's opportunity of seeing these cases. Certainly I don't think we can dismiss Lanza's work, the statistics from the Metropolitan Life Insurance Company, as to the incidence of tuberculosis among silicotic miners of all types, as compared to its incidence in the same community among people of the same social status. The difference is so remarkable, the figures for silicotics running as much as seven and ten times as high as for the others, that I doubt whether any relatively casual observations of a local group, as here reported, would shake my faith for a moment in the fact that silicosis is a predisposing cause of tuberculosis.

Gage Clement, M.D. (*closing*): I began my paper by saying that the knowledge of silicosis which I have is confined entirely to certain mining industries in the north central part of the United States. I know nothing whatever about silico-anthracotuberculosis as reported in the literature, and I know nothing whatever about asbestosis, and upon those subjects I cannot speak.

Dr. Rigler mentioned the fact that he had three deaths in which the lung was so fibrotic that it caused an extra load to be placed upon the right heart and the patients apparently died from that cause. The fibrosis from silicosis is nodular. If

there is a fibrotic condition of any other type, it is probably evidence of past infection. I have never seen a death from simple silicosis.

As to the incidence of infection, I purposely did not mention that as I wanted to confine myself to simple silicosis. Much has been written about silicosis but on reading the papers and looking at the pictures one discovers that they have to do with silicosis plus infection. I have data on silicosis with infection—films of men who have second- and third-stage nodulation, who have had broncho-pneumonia and lobar pneumonia. In the early days of this work, in following these patients, we were very much worried for fear that they were going to be disabled for life. Gradually the evidence of infection disappeared, although much more slowly than in a non-silicotic person.

Dr. Rigler mentioned predisposition to disease. I have not seen that. The statements I made in the text of my paper are true so far as we have been able to check up the incidence of tuberculosis. We have tried to trace back along the lines suggested by Dr. Wasson for the first evidence of disease, studying the chests and sinuses, and now the stomachs, of infants and children. We can carry these people back over a period of ten years, and so far we have never been able to prove that silicosis contributed in any way to any disease from which death eventually occurred.

As to whether or not silicosis may contribute to tuberculosis, I think it is quite commonly believed that tuberculosis begins rather early in life. We have the feeling that the patient has tuberculosis before he is exposed to silica dust. We have not been able to prove that the silica dust in any way aggravates tuberculosis. In some cases we have even thought it might have retarded it.

When one sees several hundred miners with second- and third-stage silicosis, perfectly healthy, perfectly well, doing just as other people in the community do, it is pretty hard to convince oneself that these people have any disability.

Factors Involved in the Production and Development of Silicotic Lesions[1]

WILLIS S. LEMON, M.D.

Division of Medicine, Mayo Clinic, Rochester, Minnesota

ALL PARTICULATE materials entering the parenchyma of the lung are disposed of in essentially the same manner. Most are dissolved, neutralized, digested, or destroyed by the cells of the tissue-cell system. Others are sequestered into nodular concentrations of cells which remain permanently or undergo changes leading to dispersion or destruction and ultimate elimination. There are many particles, both organic and inorganic, that are segregated into nodules. Of the inorganic substances, silica (SiO_2) is the most important because it constitutes the greatest hazard in the dusty trades; of organic substances, the *Mycobacterium tuberculosis* is the most important because it is the cause of a disease of major importance to man and animal alike. If this organism could be robbed of its reproductive powers, its virulence, and the allergic reactions it engenders, the response of the reticuloendothelial system to its presence would be substantially the same as that which occurs when silicon dioxide is present.

Silicosis will be discussed here under three main subdivisions: (1) the specific activator of the disease, (2) the specific cell defending the lung against damage, (3) the protective mechanisms employed by the lung to remove or segregate the dangerous particles.

THE SPECIFIC ACTIVATOR OF THE DISEASE

Etiologic Importance of Silica: Collis stressed the importance of industrial dusts containing high concentrations of silica. It was his view that no other dust was important as a cause of "dust phthisis." Ten years later Riddell said that the disease silicosis could be caused by any given dust only so far as this dust contained silica. Twenty-one years after Collis's important pronouncement Gardner (5), commenting on the similarity of the lesions of silicosis and tuberculosis, said: "In human cases where the two conditions are frequently associated it is often impossible to be certain of the etiology of a particular lesion." He was impressed by the close similarity in the tissue response to silica and to the *Mycobacterium tuberculosis* and stated: "It is remarkable that a simple inorganic compound such as dioxide of silicon (SiO_2) can set in motion a complicated series of cellular reactions comparable to those produced by a living organism made up of proteins, carbohydrates, and lipoids." Higgins and I, by means of intratracheal (9, 10, 11, 12) and intraperitoneal (13) injections, satisfied ourselves that silicon dioxide is the specific cause of the disease silicosis. We found that graphite, sericite, asbestos, granite, and other substances containing silicon dioxide in small concentrations did not, under experimental conditions, produce specific nodular fibrosis, but rather a generalized fibrosis as seen in many other conditions classified under the general term, "pneumoconioses."

Concentration of Dangerous Dusts: There appears to be a definite relationship between the concentration of air-borne dust and the production of silicosis. This does not depend on the total number of particles in the air but on three other factors: stages of dustiness, the number of very fine particles, and the content of pure silica. Mavrogordato (14), discussing the problem in the mines of the South African gold fields, thought that the same rate of production of the disease and almost the same duration of exposure for its production obtain within wide limits of dust concentration. It is not the reduction in concen-

[1] Read before the Fifth Annual Conference of Midwest Radiologists, Rochester, Minnesota, Feb. 14 and 15, 1941. Accepted for publication in June 1941.

tration of dust particles of all sizes that is of major importance. The important factor is the reduction of the concentration of those particles of silicon dioxide that are of minute size. These are infinitely more difficult to remove than are particles 10 microns or more in diameter, which are relatively harmless. Higher concentrations of dusts simply add to the numbers of larger and harmless particles. The degree of concentration of harmful dusts may, however, be reduced to a level of safety. It is a hypothetic level at which dust conditions will no longer prejudice the health of miners during a reasonable period of working life.

In discussing the hazards of workers in the hard coal industry, the authors of "Anthraco-silicosis among Hard Coal Miners" in *Public Health Bulletin No. 221* (22) reported on morbidity rates arising from exposure of miners to various concentrations of particles and the percentage of quartz in such concentrations: "Analysis of the data for the purpose of determining safe limits of dust exposure indicated that employment in an atmosphere containing less than 50 million dust particles per cubic foot would produce a negligible number of cases of anthraco-silicosis when the quartz content of the dust was less than 5 percent. In the gangways where the silica content of the dust was about 13 percent, a safe limit appeared to be 10 to 15 million particles per cubic foot. The limit of toleration for rock workers was set tentatively at 5 to 10 million particles per cubic foot of air."

Dilution: For many years observers believed that diluents such as coal dust diminished the liability of exposed miners to clinically active tuberculosis. The same idea was applied to silicosis, and for years it was accepted as fact that coal dust acted as an inhibitor to the action of silica. Clinical studies and experimental findings seemed to substantiate the concept that diluent dusts either prevented, delayed, or modified the action of siliceous dust. Heffernan believed that clay dust protected the lungs of Derbyshire miners. In 1936 Miller and Sayers (17) and in 1938 Gardner and Durkan (6) studied the question experimentally, and the latter authors wrote: "The evidence indicates that particles of other minerals mixed with silica in the form of dust tend to inhibit the inhalation of such silica and to some extent neutralise its injurious effect upon the body." They believed that the mixture of silica with other minerals modified the form of the resultant lesion and that "physical or chemical reactions between silica and inhibitor particles already inhaled into the lungs may prevent or retard the development of fibrosis." In Ontario, Denny, Robson, and Irwin studied the inhibiting effect of metallic aluminum. They reported: "The action of metallic aluminium on inhaled quartz is a local one in the lungs and is not systemic, as the inhalation of quartz + 1 per cent. metallic aluminium does not produce fibrosis, while the inhalation of quartz dust produces fibrosis in the lungs of rabbits that have been fed metallic aluminium or had it injected intraperitoneally or intramuscularly." They observed that metallic aluminum will inactivate quartz when the former is inhaled as a mixture or separately before or after inhalation of the latter. Their experiments on the minimal dosage of metallic aluminum necessary for inactivation of quartz suggest that 1 per cent of metallic aluminum is a safe minimal quantity.

When Higgins and I introduced particles of gray granite into the lungs of rabbits by intubation, we were unable to obtain typical fibrotic lesions of silicosis, but we could obtain them when we used pure silica. The same results were obtained when these materials were injected intraperitoneally. When studying the reactions of quartz from the Kolar gold mines, we obtained one sample gray in color and another white; the former contained a lower percentage of pure silica than the latter. The gray quartz was ground and the particles were suspended and injected intraperitoneally. These did not produce characteristic silicotic nodules.

When the pure white quartz was similarly treated it produced fibrous nodules comparable to, although fewer and smaller than those obtained when pure silica had been used in controls.

On the basis of all experimental evidence at hand it seems possible to say, with some degree of certainty, that mixing of other dusts with silica may serve to produce inhibitors and may modify the form of the resultant lesions.

Characteristics of the Silica Particle: All observers are in agreement as to the size of the particles of silica that cause damage by becoming arrested within the lungs: they must not be too large to prevent phagocytosis by the mononuclear phagocytic cells. The extreme limit in size is 10 microns, and in well ground quartz and in the dust of mines and dusty trades these large particles are relatively few. Badham found that samples of dust obtained in the sandstone industries were distributed according to the following sizes: 52.7 per cent measured 1 micron; 25.6 per cent 2 microns; 7.21 per cent 3 microns. Only 2.09 per cent exceeded 3 microns, and only 0.18 per cent reached a diameter of 10 microns. The dangerous particles of silica were therefore shown to be about the size of the *Mycobacterium tuberculosis*, which varies in width from 0.3 to 0.5 microns, and in length from 1.2 to 3.5 microns, but which may attain to a length of 8 microns. To be most effective and dangerous, the particles must measure from 1 to 3 microns. Of the particles below 1 micron, less certain knowledge is obtainable. It is possible that these extremely small particles pass in and out of the lung with the air inspired or expired. Those that become arrested are probably very damaging because the degree of damage is, within certain limits, inversely proportionate to the size of the particle.

Badham found in dust clouds of quartz and sandstone, both in working and experimental conditions, that "the size-frequency of particles in such dusty air corresponds closely with the size-frequency found in silicotic lungs by Watkins-Pitchford and in sputum by Philip Drinker, which are said to agree with those found in guinea-pigs' lungs, the subject of experiment by Smith and Iszard."

Badham further wrote: "(*a*) If every individual particle is equally dangerous, that is, if each particle may initiate a fibrotic condition then the 1-micron particle is the most dangerous, because it is in the majority. (*b*) If the condition of fibrosis is brought about by chemical reaction depending on the solubility of dust particles in the lungs (as is generally agreed), then the 2-micron particles are the most pernicious, this size exposing the greatest percentage of surface. (*c*) If the quantity (*i.e.*, either volume or weight) of dust is the most important factor, then the size of 3 microns is the most pernicious, this size contributing the most weight. If the number, surface and weight are each factors, then sizes 1–3 microns are the most dangerous."

Heffernan has stressed the importance of the action of electrochemical charges emanating from the surface of the phagocytosed particles. There is, however, too little exact information on the subject to warrant the forming of positive opinions. The nature of all the forces at work in the production of the disease is still unknown. The siliceous material ground and prepared for us by Dr. A. E. Osterberg fulfilled all the requirements referred to by Badham. This material produced classic lesions when introduced either into the lungs or into the peritoneal space.

THE SPECIFIC CELL DEFENDING THE LUNG AGAINST DAMAGE

When the lung is attacked by any noxious agent, organic or inorganic, it meets the attack in essentially the same way and with the same mechanism of defense. The first cells to respond are derived both from the blood by migration and from local fixed tissues. Under stimulation the cells of the fixed tissue mobilize, become active, and by chemotactic, osmotic, or electrotropic influences pass, by ameboid movement, to the affected part (16).

When the irritant is bacterial, both polymorphonuclear and mononuclear cells migrate through the walls of the blood vessels and appear at once at the point of irritation. They come in great numbers, but the neutrophils live for only a few hours. After about seventy-two hours they are replaced by increasingly large numbers of mononuclear cells, which then constitute the chief cellular defense mechanism. When particulate silica is the noxious agent, the polymorphonuclear leukocytes are less in evidence and the large mononuclear phagocytic cells predominate numerically from the beginning. The cell which is most effective in defense against silica is known as the "macrophage," or the "alveolar" phagocyte, or the "pulmonary dust cell."

When suspended organic or inorganic particles were introduced into the lungs of rabbits by way of an intratracheal catheter, they reached the subpleural alveoli within three or four minutes (9, 10, 11, 12). They promptly produced an inflammatory response, bringing in serum from the vessels, effective in the promotion of phagocytosis by two types of phagocytic cells: (1) the polymorphonuclear leukocytes, which are the first phagocytic cells used in defense, and (2) the mononuclear cells, which are less effective but which may become transformed into histiocytes. When the particulate irritant is bacterial, these cells derived from the blood are early and energetic phagocytes. These polymorphonuclear leukocytes live only a few days, then degenerate and die. In pyogenic diseases there seems to be no limit to the numbers brought to the point of invasion; but in silicosis the effectiveness of these polymorphonuclear leukocytes as defensive agents seems minimal. Higgins and I found ingested particles of silica within the polymorphonuclear cell in only one instance. The factors necessary for the promotion of phagocytosis are the opportunity for collision between a particle and a cell and the presence of serum; yet when such factors are present, these cells which avidly phagocytose carbon particles and the *Mycobacterium tuberculosis* are not phagocytic for particles of silica of the same size.

Within a few hours after the particulate material reached the alveoli, phagocytosis of all particles by macrophages was complete. The noxious element was then intracellular and became subjected to the disintegrating properties of the cellular protoplasm. Heffernan thought that the damage produced by intracellular silica is related to the electrochemical charges on the surface of the particle. Gye and Purdy thought that the damage caused results from the chemical reactions generated between the cytoplasm and the particulate invader. Maximow believed that intracellular reactions are always chemical in nature. Actually, the reaction of silica and protoplasm which results in specific fibrosis is not known with any degree of certainty.

PROTECTIVE MECHANISMS EMPLOYED BY THE LUNG

Silicosis as a disease does not occur because silica is breathed into the lungs, but rather because sufficient dangerous particles are retained within the lung. The disease represents a defect of the defense mechanisms resulting in arrest of the phagocytes after phagocytosis has taken place, and formation of the specific fibrous nodule represents the effort of the organism to segregate and localize and encapsulate the noxious substance so that the least possible degree of harm may result to embarrass respiratory function. Phagocytosis takes place largely in the alveoli, not in the larger air passages, and it is from the alveoli that the process of elimination begins. The laden phagocytes float in the serum escaped from the capillaries, or they migrate along the walls of the alveoli by ameboid movement. Within a few hours they may be seen to crowd about the terminus of the alveolar duct, which is their first intrapulmonary point of arrest.

Two paths of exit are available for these laden cells. First, they may enter the bronchiolar lumen, where changes in pres-

sure and size of the air ducts hurry them along toward the bronchi. Ciliary movement, entanglement in mucus, and muscular action form the laden cells into a bolus which is readily expelled by cough. Some observers have suggested that peristalsis of the bronchi may assist in such a mechanism of removal. The particles that find exit obviously do not become arrested and do not produce lesions.

The second route for removal of these cells is by way of the lymphatic vessels. Miller (18, 19, 20) has charted their course through the lung from their source at the terminus of the alveolar duct until they pass outside the lung to the lymph nodes at the hilus, from which they connect with the lymphatic vessels that course through the mediastinum. This lymphatic system is composed of two parts: one superficial and passing toward the pleura, and one deep, following the bronchi and blood vessels toward the hilus. It is always along these systems that arrest occurs and lesions develop. Laden cells constantly arrive at the terminus of the alveolar duct, and the irritation and stimulation of connective-tissue elements constantly augment their numbers. Cells containing mitotic figures give evidence that silica promotes hyperplasia in the tissue-cell system. Not all of these cells can be removed, and many become arrested and form aggregations that create the first cellular lesions, which are ultimately transformed into fibrous pseudotubercles. Many such laden cells enter the superficial lymphatic system and are carried in the lymph toward the periphery, where they enter the pleural plexus. Thus, anywhere along the interlobular fissures, aggregations may be formed in the course of the pulmonary vein. These were seen in our experimental sections within two weeks' time, as small, white, palpable nodules beaded along the radicles of the pulmonary vein. They are visible on the surface of the pleura at the pleural source of the vein and from their position immediately below the pleura in the course of the pleural lymphatic vessels. The pleural lymphatic vessels carry ingested particles to the bronchopulmonary and tracheobronchial nodes at the hilus, where arrest and concentration of cells create cellular nodules. In silicosis, the laden phagocytes are not readily destroyed; they ultimately become changed into white fibers and so create in these several situations true silicotic pseudotubercles. The mononuclear phagocyte is capable of many morphologic changes, but it is predestined ultimately to become a white fiber, and this transformation is final and irreversible. Permanence of the silicotic pseudotubercle depends on this metamorphosis, which changes a loose concentration of cells into a dense, fibrous nodule.

The laden cells may enter deep lymphatic vessels and pass down the center of the primary lobule along the bronchioles and pulmonary artery, rather than along the interlobar fissures to accompany the pulmonary vein to its source. There is, therefore, a drift of laden cells through the depths of the lung in the former route and a pleural drift in the latter. Higgins and I have seen these deep lymphatic vessels crowded with laden phagocytes throughout their whole course from the ductus to the hilus. They pass over and around or directly through the lymphoid tissue at the points of bifurcation of the bronchi or they divide into a plexus within the follicles, reunite, and proceed toward larger bronchi. Cellular arrest occurs in the course of the lymphatic vessels and as a result peribronchial and perivascular pseudotubercles are created. Sections made at the end of two weeks after intratracheal administration of particles, when the lesions are still cellular concentrations, show that these are usually eccentric to the bronchial lumen although they may encircle either the bronchus or the blood vessel. Lymphoid tissue is always more clearly related to the bronchus, however, than to the blood vessel, whose function is more effective in the removal of soluble substances than particulate inorganic materials.

Simson has very clearly demonstrated the situation of pseudotubercles by making

reconstruction models. His method is more nearly accurate than the macroscopic study of material or histologic study of single sections. He was surprised, however, to discover how nearly accurate the older observations proved to be and how few changes need be made in forming a true picture of the distribution of such lesions in the lung.

Through the elimination process, stimulation of the tissue cells continues and early fibrosis occurs along the routes taken by the lymphatic vessels. The roentgenologist describes this phenomenon as "a linear phase produced by peribronchial thickening and enlargement of the hilar lymph nodes." The linear shadows and the hilar enlargement may represent to him the earliest evidence of silicosis, but such evidence is not conclusively diagnostic because it is similar to that produced by many types of inorganic or even organic particles.

Kirklin and Camp made roentgenograms for me of microscopic sections of silicotic lesions experimentally produced. These permitted a roentgenologic diagnosis of silicosis only when the lesions were true pseudotubercles, discrete and lying within normal parenchyma, producing the classical nodular appearance on the roentgenogram. These roentgenograms represented shadows of single nodules; there was no confusion arising from the shadows of many superimposed nodules, such as occurs when a roentgenogram is made through the whole thickness of the lung. The less discrete lesions obtained from the use of silicates produced a more indefinite "shadowy" or "granular" appearance on the roentgenogram, which in instances of the disease among human beings had been described as a "diffuse, hazy cloudiness obscuring normal lung markings" (2).

This appearance is no more conclusively diagnostic of true silicosis than are the linear thickening and hilar enlargement previously mentioned. Both are suggestive only. Nodular, discrete shadows created by subpleural, perivascular, and peribronchial lesions usually are pathognomonic of silicosis.

Like the primary lesions of pulmonary tuberculosis, all silicotic lesions, regardless of their duration, are subject to changes that operate both within and from the outside of the nodule. When the first concentration of cells forms a microscopic nodule, pressure changes within the lung pack the cells so closely together that they assume a spherical shape. Higgins and I found that within a week the cells in the core of the nodule began to undergo degenerative changes, and when they were specifically stained, they held within their cytoplasm large numbers of small droplets of fat. Strachan and Simson have made similar observations in instances of silicosis in man. They wrote: "The silicotic process is a fibroblastic reaction followed by a dense fibrosis of nodular type, in which fat accumulation occurs in all stages and increases *pari passu* with the size of the nodule." The amount of degenerative change seemed to depend also on the numbers of particles that had been ingested, just as the degree of degenerative change in the tubercle depends on the number of virulent organisms of tuberculosis within the phagocytes. Both particles of silica and the organisms of tuberculosis are protoplasmic poisons and under experimental conditions both cause fatty degeneration. Later, we found, the core of the nodule became hyaline in character or, as in the tubercle, calcium settled there and formed calcified lesions.

Within a few weeks' time, the pseudotubercles which had developed in the lungs of our experimental animals had attained a diameter of 1 to 3 mm. and were palpable and visible on the pleural and cut surfaces of the lung. In roentgenograms of the microscopic section the lesions were discrete and nodular, small, medium, or large, and surrounded by normal parenchyma. Emphysematous parenchyma often surrounded lesions that had been developing for a period of three or four months. Very large shadows in roentgenograms represented conglomerate lesions which, in

the absence of infection, were formed by crowded, separate, and discrete pseudotubercles.

The exact situation of particulate silica within the lung may be studied by means of the polarizing microscope and by the incineration of unstained tissue 15 microns in thickness. McHeffey has studied such material obtained from human beings, and he and I are undertaking a similar investigation of experimental silicosis. The polarizing microscope shows that the particles are most numerous in the core of the nodule and that they become progressively fewer toward the periphery. When the nodule is in the process of development and there is an uninterrupted drift of laden cells toward the lymphatic depots and the immature nodules, many laden cells can be seen in surrounding tissue. These cells lie free in the perinodular alveoli and in the finer divisions of the bronchioles. Similarly, when the nodule is degenerating, the dead cells shed particles which are again phagocytosed and are often seen just peripheral to the nodule. Nodules of different duration may frequently be found in the same section and constitute evidence of the constant changes that tend to destroy them, whether they be of short duration and still cellular or of long duration and seemingly obliterated by concentric fibrous envelopes or calcification of the core. In our experiments only one intratracheal injection was made, so that there was no continuous addition of particles from outside sources. All peripheral particles must have been derived from the nodules themselves in the course of their disintegration. Such observations support the belief that silica is always continuous in action, and there is no time limit to the duration of the disease, silicosis, in which silica is the specific etiologic agent.

Under prolonged and continuous stimulation, even in the absence of superimposed infection, fibrous changes proceed. Within a year, in one of our animals, a lobe of the lung became almost completely fibrotic. Mavrogordato (15) has said that silica stimulates production of macrophages and fibroblasts and sends the whole reticuloendothelial system "fibre-ways," with the development of true hypertrophy. The particular lobe of the lung of the animal with which we worked was hard, white, and roughly nodular. Microscopically discrete pseudotubercles created large conglomerate nodules, and all the perinodular pulmonary tissues were involved in fibrotic changes: the alveolar walls were thickened, the alveoli were compressed, and the bronchioles were deformed into slit-like fissures which it was possible to identify only because their mucosa and muscular layers had been preserved. These structures were separated by heavy layers of dense fibrous tissue. The lungs resembled those described in advanced simple silicosis in the lungs of old Cornish miners who were dyspneic and cyanotic as a result of the damage to the capillary bed and the resultant strain on the right side of the heart.

When infection supervened, however, we observed the resultant changes to be similar to those seen in tuberculosilicosis among human beings or even in simple fibrocaseous tuberculosis. The pseudotubercles were no longer discrete but were surrounded by granulation tissue. The parenchymal structures were no longer unaffected by inflammatory change, but the finer structures were thickened and deformed and evidences of bronchitis and pneumonia were commonly encountered. As in tuberculosis, ulceration and necrosis progressed and erosion of the vessels and bronchi occurred. There was also the same tendency toward the formation of thrombi in blood vessels and lymphatic vessels that is characteristically found in tuberculosis produced experimentally by a similar intratracheal technic.

SUMMARY

Experimentally produced silicosis, like silicosis found among human beings, results from the interaction of particulate silica and the tissue-cell system of the lungs. The nature and degree of the de-

fense reactions depend upon the size, number, and mass of the particles of silica. The exact cause of the reaction is unknown, but it is probably brought about by electrochemical effects induced by contact of the particle and the cytoplasm of phagocytic cells. It probably proceeds because the laden cells are not killed but are preserved, and may be concentrated into aggregations of cells situated along the course of the lymphatic system of the lungs. Arrest occurs as a result of phagocytosis and failure on the part of the eliminating mechanism of the lung.

The pathognomonic criterion of experimentally produced silicosis is the discrete pseudotubercle, pearly white in color, glandular, subpleural or perivascular and peribronchial in situation, and visible and palpable on cut section.

The morbid changes in lungs of experimental animals are controlled by encapsulation, calcification, and obliteration by collagenous and reticular fibers. Superimposed infection increases fibrosis in the perinodular parenchyma, causes ulceration and necrosis of bronchi and blood vessels, and brings about death of the animal by bronchitis, bronchopneumonia, and empyema. Simple uninfected silicosis affects the function of the lungs in proportion to the amount of fibrous tissue that develops, the consequent reduction of vital capacity, and the secondary loss of cardiac compensation.

REFERENCES

1. BADHAM, CHARLES, RAYNER, H. E. G., AND BROOSE, H. D.: Extract from the Report of the Director-General of Public Health, New South Wales, for the Year Ended 31st December, 1927. Studies in Industrial Hygiene, No. 12. Sydney, Alfred James Kent, Government Printer, 1929, pp. 87–91.

2. COLE, L. G., AND COLE, W. G.: Pneumoconiosis (Silicosis): The Story of Dusty Lungs, a Preliminary Report. New York, John B. Pierce Foundation, 1940, pp. 45–46.

3. COLLIS, E. L.: Industrial Pneumoconioses with Special Reference to Dust-Phthisis. Pub. Health, London **28:** 252–259, 1914–1915.

4. DENNY, J. J., ROBSON, W. D., AND IRWIN, D. A.: Prevention of Silicosis by Metallic Aluminium. Progress Report Covering the Work from the Preliminary Paper, July 1937 to July 1938. In Silicosis, Proceedings of the International Conference held in Geneva from 29 August to 9 September, 1938. London, P. S. King & Sons, Ltd., 1940, pp. 208–210.

5. GARDNER, L. U.: Similarity of the Lesions Produced by Silica and by the Tubercle Bacillus. Am. J. Path. **13:** 13–24, January 1937.

6. GARDNER, L. U., AND DURKAN, T. M.: Protective Action of Various Minerals against Free Silica. In Silicosis, Proceedings of the International Conference held in Geneva from 29 August to 9 September, 1938. London, P. S. King & Sons, Ltd., 1940, pp. 108–123.

7. GYE, W. E., AND PURDY, W. J.: Poisonous Properties of Colloidal Silica. I. Effects of the Parenteral Administration of Large Doses; II. Effects of Repeated Intravenous Injections on Rabbits; Fibrosis of the Liver. Brit. J. Exper. Path. **3:** 75–85, 86–94, April 1922.

8. HEFFERNAN, P.: What is Silicosis? Tubercle. **16:** 397–405, June 1935.

9. LEMON, W. S., AND FELDMAN, W. H.: Comparison of the Development of the Specific Nodule of Silicosis and of Tuberculosis. Arch. Int. Med. **53:** 367–378, March 1934.

10. LEMON, W. S., AND HIGGINS, G. M.: Development of the Pulmonary Silicotic Nodule in the Experimental Animal. Am. Rev. Tuberc. **28:** 470–483, October 1933.

11. LEMON, W. S., AND HIGGINS, G. M.: Pulmonary Lesions Experimentally Produced by Intratracheal Introduction of Aluminum Oxide and of Borosilicate-Glass. Am. Rev. Tuberc. **30:** 548–560, November 1934.

12. LEMON, W. S., AND HIGGINS, G. M.: Tissue Reactions of the Lung to the Intratracheal Injection of Particulate Sericite. Am. Rev. Tuberc. **32:** 243–256, September 1935.

13. LEMON, W. S., AND HIGGINS, G. M.: Unpublished data.

14. MAVROGORDATO, A.: Contributions to the Study of Miners' Phthisis. Johannesburg, Publications of the South African Institute for Medical Research, No. 19, December 1926, 83 pp.

15. MAVROGORDATO, A.: Contributions to the Study of Miners' Phthisis. Johannesburg, Publications of the South African Institute for Medical Research, No. 19, December 1926, p. 16.

16. MAXIMOW, A. A.: Morphology of the Mesenchymal Reactions. Arch. Path. **4:** 557–606, October 1927.

17. MILLER, J. W., AND SAYERS, R. R.: Physiological Response of Peritoneal Tissue to Certain Industrial and Pure Mineral Dusts. Pub. Health Rep. **51:** 1677–1689, Dec. 4, 1936.

18. MILLER, W. S.: Distribution of Lymphoid Tissue in the Lung. Anat. Rec. **5:** 99–120, March 1911.

19. MILLER, W. S.: Studies on Tuberculous Infection. III. The Lymphatics and Lymph Flow in the Human Lung. Am. Rev. Tuberc. **3:** 193–209, June 1919.

20. MILLER, W. S.: Key Points in Lung Structure. Radiology **4:** 173–177, March 1925.

21. OSTERBERG, A. E.: Personal communication to the author.

22. Public Health Bulletin No. 221: Anthraco-Silicosis among Hard Coal Miners. United States Treasury Department, Public Health Service, December 1935, 114 pp.

23. RIDDELL, A. R.: Silicosis: Its Relation to Tuberculosis. Pub. Health J. **17:** 1–8, January 1926.

24. SIMSON, F. W.: Reconstruction Models Showing the Moderately Early Simple Silicotic Process and How It Affects Definite Parts of the Primary Unit of the Lung. J. Path. & Bact. **40:** 37–44, January 1935.

25. STRACHAN, A. S., AND SIMSON, F. W.: Preliminary Study of the Pathology of Silicosis as Seen on the Witwatersrand. In Silicosis. Records of the International Conference held at Johannesburg, Aug. 13 to 27, 1930. London, P. S. King & Sons, Ltd., 1930, pp. 223–248.

Twelve-Year Review of X-Ray Therapy of Gas Gangrene[1]

JAMES F. KELLY, M.D., F.A.C.R., and D. ARNOLD DOWELL, M.D.

Omaha, Nebraska

THE FIRST REPORT on the x-ray treatment of gas gangrene was made in December 1931, before the Radiological Society of North America at the Seventeenth Annual Meeting in St. Louis (1). The mortality rate for gas gangrene up to that time had been 50 per cent or higher and that figure was attained only by the sacrifice of many arms and legs. The mortality rate in the group of 8 cases then reported was 25 per cent, and no additional tissue was removed in any case after x-ray therapy was begun.

The technic used in the 6 cases involving the extremities was described and was considered adequate, but the 2 patients with involvement of the trunk died, and for the treatment of such cases heavier kilovoltage was advised. Nothing was promised but others were requested to try the method if opportunity arose. The request did not go unheeded and in the nine years which have followed the writer has witnessed an exhibition of sincere co-operation on the part of many radiologists, a number of surgeons, and a few practitioners in the other specialties.

Sufficient data have thus been assembled to permit the formation of conclusions which would have required a great number of years if left to one man's observation of this relatively rare disease.

The graph reproduced in Figure 1 shows the drop in the mortality rate of gas gangrene with x-ray therapy in a twelve-year period. It indicates that gas gangrene need no longer be regarded as a serious disease.

The use of a therapeutic measure of unknown effectiveness was justifiable in such a disease as gas gangrene with its former high mortality and morbidity. The x-ray, however, has definitely removed gas gangrene from that group of diseases in which experimental therapy is any longer justifiable.

Chemotherapy has failed in our vicinity and also in other places, as was to be expected, since in a well developed case of gas gangrene there is definite interference in the circulation to the infected area and consequently in the most serious cases the chemical fails to reach the diseased tissues. The x-ray, however, has no difficulty in effectively reaching all cells and fluids in any infected area. Other ways of treating gas gangrene may be developed but there can be no question as to the status of the x-ray in the prevention and treatment of this serious infection at the present time.

PRESENT STATUS OF THE METHOD

The mortality rate in gas gangrene cases treated with x-rays is so much lower than that obtained by other methods employed up to this time that those who refuse to use irradiation now feel called upon to offer some explanation. As a rule their reasons are centered about the correctness of the diagnosis in cases treated with x-rays.

In an attempt to clarify this situation, data relative to the origin of treated cases and their diagnoses are presented in Table I. The origin of the cases analyzed is shown in column 1, and the mortality rates for the various groups in column 2. In the remaining columns the cases are further divided according to the criteria which determined the diagnosis: in column 3 is shown the number of cases diagnosed solely on clinical grounds; column 4 lists the cases with a clinical diagnosis and x-ray evidence of gas in the tissues, and column 5 the cases in which not only were these

[1] From the Department of Radiology, Creighton University School of Medicine. Read before the Radiological Society of North America at the Twenty-sixth Annual Meeting, Cleveland, Ohio, Dec. 2–6, 1940.

TABLE I: DIAGNOSTIC CRITERIA AND MORTALITY RATES OF VARIOUS GROUPS OF POST-TRAUMATIC CASES

Column 1 Origin of Cases	Column 2 Total Cases		Column 3[3] Clinical Diagnosis Only (no x-ray films)		Column 4 Clinical Diagnosis and Gas Shown on X-ray Film		Column 5 Laboratory Diagnosis		Column 6 Method of Diagnosis Not Stated for Each Case	
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths
(A) Cases reported in the literature in detail by J. F. Kelly	12	3 (25%)	1	1 (100%)	3	1 (33.3%)	8	1 (12.5%)		
(B) Cases reported in literature in detail from other sources	37	4 (10.8%)	10	2 (20%)	3	0	24	2 (8.3%)		
Total of (A) and (B)	49	7 (14.2%)	11	3 (29.1%)	6	1 (16.6%)	32	3 (9.3%)		
(C) Cases reported in the literature, not in detail, from other sources[1]	35	2 (5.7%)					12	1 (8.3%)	23[2]	1 (4.3%)
Total cases in the literature (A) (B) (C)	84	9 (10.7%)	11	3 (29.1%)	6	1 (16.6%)	44	4 (9.09%)	23	1 (4.3%)
(D) Other cases treated by J. F. Kelly[3]	9	1 (11.1%)	1	0	3	1 (33.3%)	5	0		
(E) Cases seen in consultation by J. F. Kelly in the Omaha area[3]	31	4 (12.9%)	11	1 (9.9%)	6	1 (16.6%)	14	2 (14.2%)		
(F) Cases sent to J. F. Kelly from other sources but not reported in detail by anyone	240	28 (11.6%)	70	12 (17.1%)	26	4 (15.3%)	144	12 (8.3%)		
Total of all cases	364	42 (11.5%)	93	16 (17.2%)	41	7 (17.3%)	207	18 (8.6%)	23	1 (4.3%)

[1] Series of Williams and Hartzell; Bates; Charbonnet and Cooper.
[2] Series of Bates; Charbonnet and Cooper.
[3] Groups (D), (E), and (F) are not included in the literature in detail, appearing only in statistics.

criteria satisfied but the presence of *Cl. welchii* was demonstrated by laboratory procedure. In column 6 are cases from the literature in which the method of diagnosis was not stated.

Groups A and D in column 1 contain the authors' 21 cases treated in a period of twelve years. The 12 cases in Group A are recorded in detail in the literature; the 9 cases in Group D are reported only statistically. The mortality rate for the 21 cases is 19 per cent. Group E is made up of 31 cases seen by the author in consultation in the Omaha area, with a mortality of 12.9 per cent, and Group F of 240 cases sent to the author from other sources for analysis, with a mortality of 11.6 per cent. The 37 cases from other sources, reported in detail in the literature (Group B) show a mortality of 10.8 per cent, while the 35 cases from the literature not given in detail (Group C) have a mortality rate of 5.7 per cent.

For all cases reported in the literature, Groups A, B, and C (84 cases), the mortality is 10.7 per cent, while for 364 cases available for study from all sources, the rate is 11.5 per cent. Excluding the authors' first two deaths, due to inadequate treatment of cases with trunk involvement, the mortality rate is remarkably consistent regardless of the origin of the material.

It is of interest that the mortality rates are higher in the 21 cases treated in our institutions, the 31 which we saw in consultation, and the 240 which we analyzed and reported for others, than in the series col-

lected from the literature. It is a satisfaction to realize that we have not been misleading in our claims and that the method has in most instances been successful in other hands. It is noteworthy, also, that those cases which have been included in our statistics on clinical evidence only show a much higher mortality rate (twice as great) than cases in which *Cl. welchii* was demonstrated in the laboratory. In that in the group analyzed the error in diagnosis should not exceed 2 per cent, and we hope that it is even less. The cases reported in the literature we have accepted as given.

Anyone with clinical experience in the management of gas gangrene appreciates that the diagnosis depends on several factors, no one of which may be considered as final in the early or doubtful stages of the

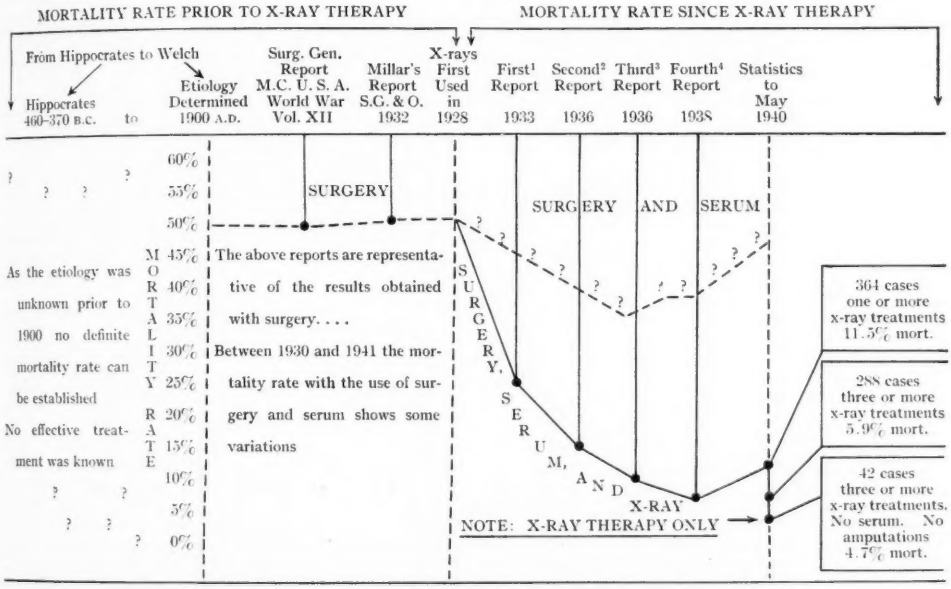


Fig. 1. End of gas gangrene as a serious infection (if x-ray therapy is used).

From Hippocrates' time (460–370 B.C.) to 1900 A.D. the etiology of gas bacillus infection was unknown and as a result the mortality rate during that period cannot be accurately determined. Between 1900 and 1928 the mortality rate was 50%. Since 1928, the mortality has been reduced to 5% by the use of x-ray therapy without serum or radical surgical measures. X-ray therapy will prevent or cure the disease. The broken perpendicular lines separate the three periods.

[1] Kelly, J. F.: Radiology **20:** 296–304, April 1933.
[2] Kelly, J. F.: Radiology **26:** 41–44, January 1936.
[3] Kelly, J. F., and Dowell, D. A.: J. A. M. A. **107:** 1114–1118, Oct. 3, 1936.
[4] Kelly, J. F., Dowell, D. A., *et al.*: Radiology **31:** 608–619, November 1938.

other words, the inclusion of cases with questionable diagnoses has raised rather than lowered our mortality rate.

We have included no case in our statistics which did not have evidence of toxemia, nor have we excluded any in which death occurred because there was a plausible pretext by which it might be rejected. Errors through rejection of true gas bacillus infections which showed no evidence of toxemia because of early x-ray treatment may have occurred, but we believe disease, which is the most important time for the diagnosis to be made.

The consistency of the mortality figures in the foregoing analysis is maintained in figures relative to other important data, and the present study will serve to verify the general trend of our previous reports.

REPORTS IN THE LITERATURE

All reports on the roentgen treatment of gas gangrene that have appeared thus far in the literature have been favorable

TABLE II: GAS GANGRENE CASES REPORTED IN THE LITERATURE*

Reference	Traumatic			Diabetic			Arteriosclerotic		
	Cases	Lived	Died	Cases	Lived	Died	Cases	Lived	Died
Kelly, J. F.: Radiology **20:** 296–304, April 1933	8	6	2						
Faust, J. J.: Radiology **22:** 105–106, January 1934	5	5	0						
Turner, B. W.: Urol. & Cutan. Rev. **38:** 153–158, March 1934	1	1	0						
Faust, J. J.: Illinois M. J. **66:** 547–551, December 1934	2	0	2						
Hanchett, M.: West. J. Surg. **43:** 199–207, April 1935	2	2	0						
Kelly, J. F.: Radiology **26:** 41–44, January 1936	19	17	2	1	0	1			
Bates, M. T.: Ann. Surg. **105:** 257–264, February 1937	5	5	0						
Anderson, R.: Surg., Gynec. & Obst. **64:** 919–926, May 1937	1	1	0	1	1	0			
Eliason, E. L., *et al.:* Surg., Gynec. & Obst. **64:** 1005–1014, June 1937	1	1	0						
Anderson, R.: Staff. J., Swedish Hosp. **1:** 70, October 1937	1	1	0						
Gambill, I., and Cupp, H. B.: M. Bull. Vet. Admin., January 1938	1	1	0						
Faust, J. J.: Texas State J. Med. **34:** 404–409, October 1938	3	3	0						
Charbonnet, L. S., Jr., and Cooper, R. W.: New Orleans M. & S. J. **91:** 335–345, January 1939	18	17	1	1	1	0	1	0	1
Buchanan, J. C.: Columbia Med. Society, Richland Co., S. C., March 1939	1	1	0						
Williams, A. J., and Hartzell, H. V.: West. J. Surg. **47:** 561–565, October 1939	12	11	1	2	1	1	4	2	2
Sewell, R. L.: Surgery **6:** 221–229, August 1939	2	2	0	2	1	1	1	0	1
McNamee, E. P., and Lulenski, C. R.: Ohio State M. J. **35:** 1062–1065, October 1939	7	6	1				2	1	1
Godby, W. H.: M. J. Australia **1:** 85–88, Jan. 20, 1940	3	2	1						
Bowen, A.: Mil. Surgeon **86:** 107–112, February 1940	2	2	0						
TOTAL	94	84	10 (10.6%)	7	4	3 (42.8%)	8	3	5 (62.5%)

* Authors' reports other than the first two have been omitted. In other instances cases have been dropped from reports to prevent duplication due to inclusion in other papers.

(Tables II and III) to the use of x-rays both as a prophylactic and therapeutic measure, with the exception of that of Coleman and Bennett (2), who reported[2] 10 deaths in a series of 14 cases. When their mortality rate of 71.3 per cent for 14 cases is compared with the mortality rate of 10.7 per cent for the 84 post-traumatic cases in the literature, 16 per cent for the 106 cases, of all types, covered by the other twenty published reports, and

[2] Read before the Section of Industrial Medicine and Public Hygiene of the American Medical Association at Atlantic City, June 11, 1937. This paper was presented before the Hubeny-McNattin report (3).

11.5 per cent for the 364 post-traumatic cases from all sources, one must question the selection of patients or the technic of treatment in a series with results so distinctly different from those obtained by others.

mize its value. Not all patients treated with x-ray recover, but in our experience and the experience of others the mortality rate in the post-traumatic cases should not be in excess of 10 per cent. When it is higher some explanation should be sought.

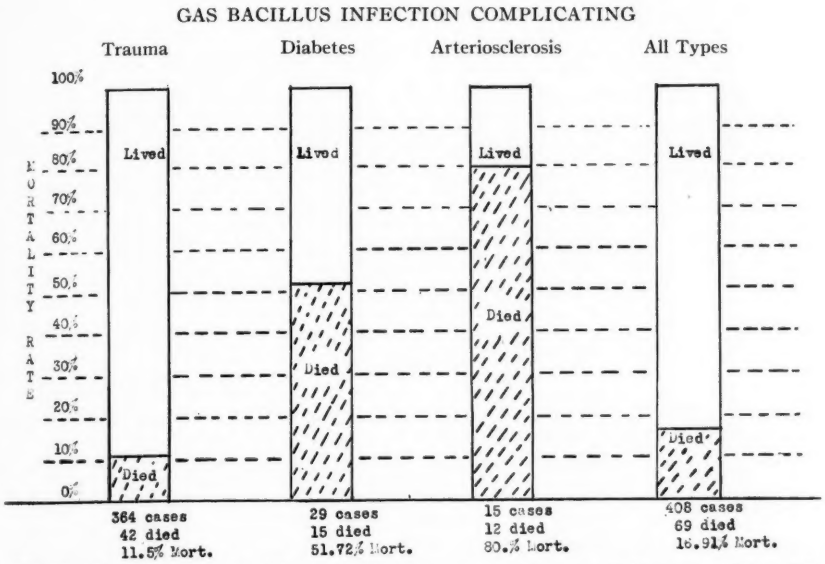


Fig. 2. Mortality rate for 408 cases, of all types, receiving x-ray therapy. These data show that the diabetic or arteriosclerotic patient who develops a gas bacillus infection still presents a very serious problem. The mortality rate of 11.53 per cent in the post-traumatic group included all cases in that group: those receiving one, two, and three or more x-ray treatments. The mortality for the group which includes all types of cases is much lower than is found in the literature but it is low because of the preponderance of post-traumatic cases.

TABLE III: RECENT REPORTS NOT INCLUDED IN OTHER TABLES

	Cases	Lived	Died
Kennedy, W. D.: Illinois M. J., March 1938	1	1	0
Newell, E. D.: Ann. Surg. **110:** 100–106, July 1939	2	2	0
Anderson, W. D., and Olim, C. B.: Memphis M. J. **14:** 189–191, November 1939	8	6	2
Von Briesen, D.: Southwestern Med. **24:** 160–161, May 1940	12	10	2
Ham, Harold: M. J. Australia, **2:** Sept. 28, 1940	5	5	0
TOTAL	28	24	4 (14.28%)

The absence of any detailed account of specific cases or technical data in the Coleman-Bennett report which can be critically examined would seem to mini-

We have never claimed that x-ray therapy will cure all the moribund patients, but we do believe, and have stated (1), that any patient, no matter how far his disease has advanced, is entitled to a trial of x-ray therapy. Not every technic is suitable for these cases, as was pointed out in our first report. Patients treated reasonably early and with the correct technic will respond favorably in most instances.

One statement in the Coleman-Bennett (2) report should not go unchallenged or it may do considerable harm. These authors write: "In the few cases responding to x-ray, wide opening and amputation resulted in recovery." In the light of our experience this statement is incredible. In the opinion of the writer (J. F. K.), amputation during the acute toxic phase of gas

TABLE IV: GAS GANGRENE: MORTALITY RATE ACCORDING TO AREA INVOLVED

	Total Cases	Lived	Died	Mortality
Extremity cases	303	275	28	9.2%
Trunk cases	51	37	14	27.5%
Undetermined	10	10	0	0.0%
TOTAL	364	322	42	11.5%

bacillus infection which is receiving adequate and proper x-ray therapy has never benefited any patient in the least. Under such conditions recovery ensues in spite of the amputation and not because of it. (See discussion on amputation.)

The figures presented by Coleman and Bennett must be considered in relation to the other twenty reports in the literature, totalling several times as many cases. Thus less harm will come from such a report.

For a more recent opinion as to the use of x-rays in treating gas gangrene at Cook County Hospital, where Bennett states he treated the majority of his cases, the reader is referred to the report of Hubeny and McNattin (3) of the present radiological staff in that institution. They state:

"*Gas Gangrene—Erysipelas.* Two more formidable complications can scarcely be asked for, and yet, withal their devastating aggressiveness, they can be throttled very effectively with irradiation therapy. The only cases we have lost, especially in the series of patients suffering from gas infection, have been those who have been sent to us in a semi-moribund state, postoperative, with crepitus involving half of their body and temperature of 104–105° F.

"We urge all those who read this article never to hesitate to recommend X-ray therapy for any patient whom you suspect of having gas infection or erysipelas. If there is ever any emergency X-ray treatment needed, regardless of the time of day or night, it is for the treatment of either of these diseases."

During the entire time x-ray therapy has been used for prevention and treatment of gas gangrene, no unfavorable report has come to our attention, from any source, if treatment was in accord with our technic.

Table III lists a number of reports brought to our attention during the past few months, which have not been included in any other tables or graphs in this paper. The addition of these new cases, while it would not materially alter our results, might yet give the adherents of chemotherapy an opportunity to charge us with too frequent shift of statistics to be properly checked.

AMPUTATIONS

As stated early in our reports, we are strongly opposed to amputation and débridement for the prevention and treatment of gas gangrene infection. In other words, we believe that whatever surgery is indicated because of the injury should be performed but there should be no extensive removal of muscle groups or other major surgery for the infection itself during the acute toxic phase.

With x-ray therapy there is no necessity for attempting to estimate the extent to which the gangrene will progress during the invasive stage since the tissue which is destroyed during this time becomes demarcated as the disease regresses, and the dead tissue, if there be any, may be removed after the acute toxic stage has passed. There should not be over a 1 or 2 per cent mortality because of deferred amputation and about the same mortality from the infection itself. Prophylactic irradiation is indicated after the secondary operation.

For the mortality in the different groups with relation to amputation, see Figure 3.

In the post-traumatic series there were 303 cases in which the extremities were chiefly involved, 51 cases with trunk involvement, and 10 cases in which the area of major involvement was not determined. The significance of the figures in Table IV is more thoroughly appreciated when one realizes that the circle (Fig. 3) represents 303 cases with involvement of the extremities or 83 per cent of the total post-traumatic group, and that in only 27.3 per cent (66 out of 242 cases) was amputation done as a therapeutic measure. This is far below the usual percentage of therapeutic amputations in post-traumatic cases

of gas gangrene not treated with x-rays. The mortality rates both in the amputated (12.12 per cent) and *non*-amputated (8.5 per cent) groups are much lower than those usually reported for series of cases not receiving x-ray therapy; hence the objection to their trial, but the reverse is true: we are advocating the use of a simple and effective measure to replace drastic measures which are ineffective.

Previously there has been no treatment for the infected part in gas gangrene, since

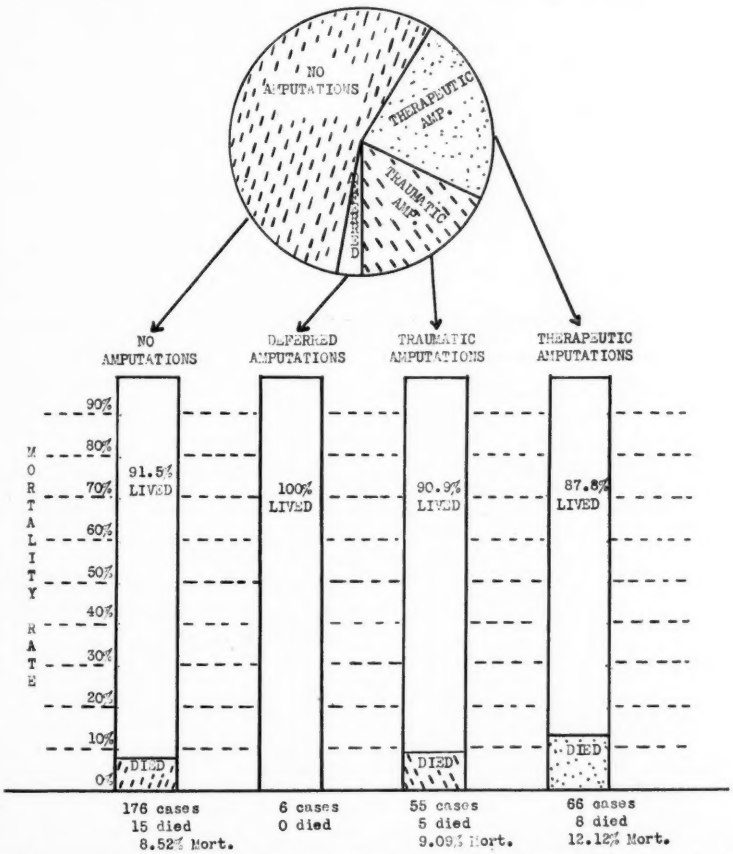


Fig. 3. The circle shows the recent trend away from therapeutic amputations. The pillars show a higher mortality rate in the therapeutic amputation group as compared with other groups. These data show that amputation as a therapeutic measure during the acute toxic phase is a factor in increasing the mortality rate in gas bacillus infection. This is a consistent finding in all series of cases treated with x-ray up to this time. Amputation is an obsolete therapeutic procedure for gas bacillus infection. It has no therapeutic value and adds to the morbidity and the mortality. Less than 22 per cent of the total number of cases had therapeutic amputations.

absence of major surgery has not raised the death rate. This is the answer of the radiologist to those who claim that without early amputation the patient must die. If we were advocating the use of drastic measures to replace a simple and effective procedure there might be a reasonable amputation, or elimination of the infected area by surgical measures, can hardly be considered treatment. It was in the past an occasional means of saving the patient's life, but the area involved was not treated; it was simply removed. With x-ray therapy the infected part is actually

treated and is removed only if it does not recover.

It is not intended to convey the impression that no other successful method of preventing and treating gas gangrene will ever be found, but at the present time x-ray therapy, as far as we have been able to determine, is far superior to any other method. When it is available, questionable and experimental measures of whatever character should not be used.

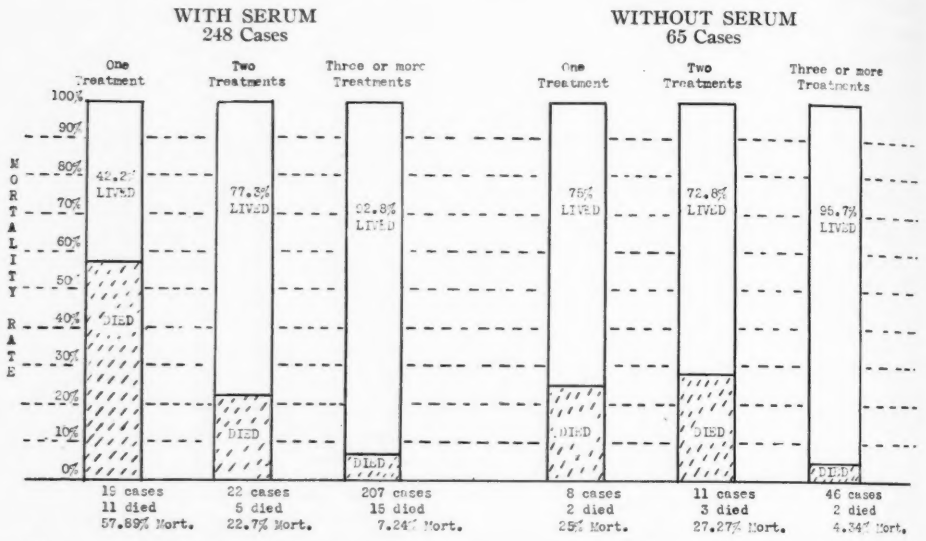


Fig. 4. Mortality rate of 313 post-traumatic gas gangrene cases according to the number of x-ray treatments, with and without serum. The graph illustrates the advantage of early x-ray therapy. The use of serum is not necessary if x-rays are used. The lowest mortality is in that group of patients receiving no serum and three or more x-ray treatments.

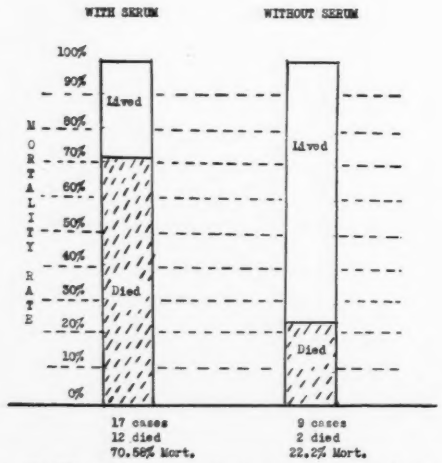


Fig. 5. Diabetic patients who developed gas gangrene and received x-ray therapy. These data, though not extensive enough to warrant final conclusions, suggest that probably patients who have a gas bacillus infection complicating their diabetes do better without serum than with serum when treated with x-ray.

SERUM

In the first report the hope was expressed that if x-rays proved successful in treating gas gangrene less serum might be used. The records of some deaths, particularly among diabetic patients, would suggest that the serum may have been an important factor in the fatal outcome. The many instances in which serum has failed to prevent or cure the disease, while x-ray therapy has been followed by prompt improvement, give the impression that if x-rays are available serum is unnecessary.

Large doses of serum after the kidneys have been damaged by the toxin of a gas infection appear to be more than some patients can withstand, and urinary suppression and death ensue.

Use tetanus antitoxin.

From Figure 4 it is evident that the mortality rate is lower when serum is omitted than when it is used. In the usual post-traumatic cases the difference is not great, but among the few diabetic patients we have available for study it is quite marked (Fig. 5).

PROPHYLAXIS

Very early in this study it was evident that x-rays might also have a prophylactic value. Later they were used successfully by several workers to prevent gas gangrene and it was observed that the incidence of other infections also, osteomyelitis after compound fracture in particular, seemed lessened by their use.

No reason is suggested for the action of x-rays in preventing osteomyelitis, but if the rapidly growing organisms, such as the gas formers and the streptococci, can be kept from establishing an infection immediately after the injury, it is possible that the more stubborn slowly growing secondary invaders will never have an opportunity to develop, as the wound may be well on the way to recovery before their usual period of incubation has been completed.

For the past several years it has been our custom to give one treatment each day for three days as a prophylactic dose. Excellent results have thus been obtained. Figure 6, indicating the time of onset of gas gangrene, shows the prophylactic dose to have been given at the most opportune time. In this graph the greater number of cases are seen to have their onset between the twenty-fourth and the ninety-sixth hour after injury, with the peak between the forty-eighth and the seventy-second hour. It would also appear from this figure that the earlier the onset the more virulent the disease, as the mortality rate during this early period is definitely higher than at other times. It is probable, however, that many of the patients died of their original injury, as a result of hemorrhage, shock, or other cause.

In spite of the fact that the severity of

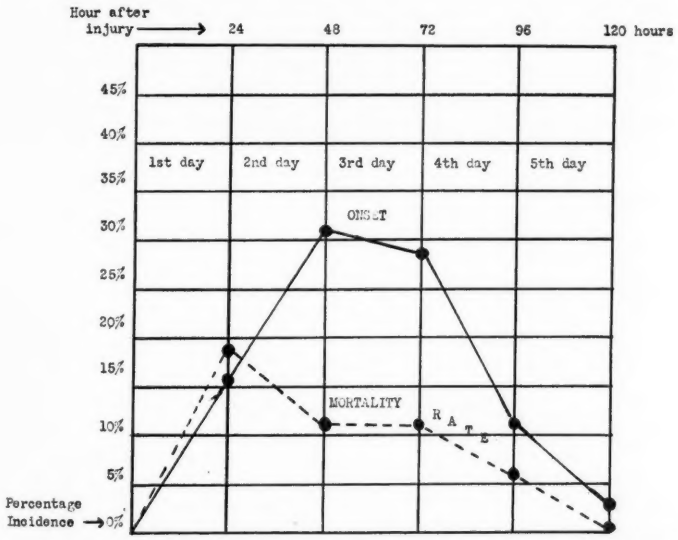
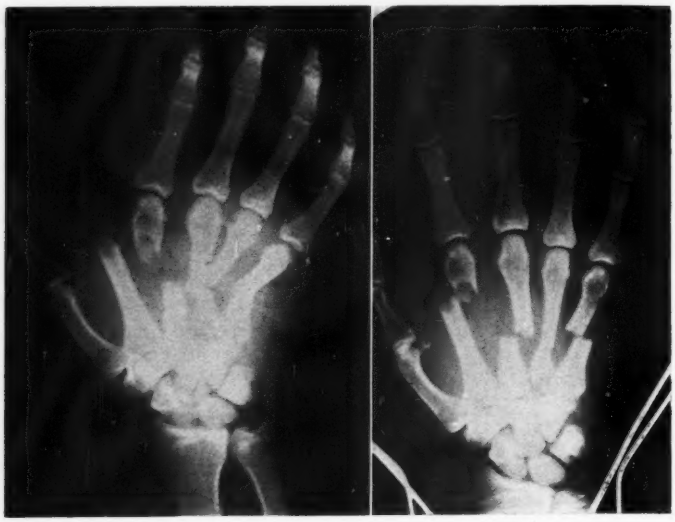


Fig. 6. Incubation period of gas gangrene in 134 available cases; also the mortality rate according to the time of onset. The time of onset of gas gangrene is figured on a 24-hour time interval after injury, and this is designated by the solid line. The greater number of cases have their onset between the 24th and the 96th hour after injury, with the peak between the 48th and the 72nd hour. The mortality rate in these same cases is designated by the broken line in the graph.



Figs. 7–8. Case 1: Severe hand injury, with multiple compound fractures and some gas in tissues (left). Fig. 8 (right) shows same hand a few days after prophylactic x-ray irradiation: no gas in the tissues, no infection, hand on way to complete recovery.

TABLE V: CASES WHICH RECEIVED PROPHYLACTIC IRRADIATION AND HAVE BEEN REPORTED IN THE LITERATURE

	Cases Which Received Prophylactic Irradiation	Cases Which Developed Gas Bacillus Infection after Prophylactic Irradiation
Bowen, A. A.: Mil. Surgeon **86:** 107–112, 1940	39	1
Anderson, R., and Wirth, J. E.: Staff J., Swedish Hospital, Seattle, Wash. **1:** 70, 1937	1	0
Charbonnet, L. S., and Cooper, R. W.: New Orleans M. & S. J. **91:** 335–345, 1939	8	0
Kelly, J. F., and Dowell, D. A.: Radiology **32:** 675, June 1939	9	0
McNamee, E. P., and Lulenski, C. R.: Ohio State M. J. **35:** 1062–1065, 1939	2	1
Williams, A. J., and Hartzell, H. V.: West. J. Surg. **47:** 561–565, 1939	7	0
Anderson, W. D., and Olim, C. B.: Memphis M. J. **14:** 189–191, 1939	24	0
TOTAL	90	2

the injury is undoubtedly a factor in these early deaths, we are of the opinion that the infections which are evident a few hours after the injury are more virulent than those which do not appear until three or four days have elapsed. It is evident from Figure 6 that the second, third, and fourth days are the most effective for prophylaxis as it is during that time that the onset of the disease is most frequent. This does not mean that the use of the x-ray for prophylaxis on the first day would not be preferable, but automobile and other accident cases are usually first seen on the second day or even on the third day after injury, and prophylaxis under these circumstances has been satisfactory.

The disease which starts after the third or fourth day is of relatively low virulence if the mortality rate in the few cases in this group is maintained when larger numbers are available for study. Among the 30 cases diagnosed after the seventy-second hour there were only two deaths, a mortality rate of 6 per cent.[3]

Table V lists several series of cases reported by others which received prophylactic irradiation. While these are only a small percentage of the cases which have

[3] This particular analysis of our material was made at the request of Lt. Col. H. W. Grady and Major A. A. de Lorimier of the Medical Corps of the United States Army.

actually received such treatment, they nevertheless show that physicians in widely separated parts of the country are already giving this method a trial.

A Nebraska orthopedic surgeon (4) may be quoted as follows: "Give a prophylactic dose of x-rays twice daily for three or four days over every compound fracture . . . . I have followed this practice in nearly every case for the past few years and as a result I know little regarding this complication except what appears in the literature . . . . "

As indicated by Dr. Thomson's remarks there are a great number of cases in which prophylactic x-ray irradiation has been done after compound fractures and similar injuries, which have never been reported.

CASE 1: R. P., white male, age 18, entered the hospital four hours after his hand was mangled in a corn picker, causing a compound fracture of the second, third, fourth, and fifth metacarpals. The x-ray film showed considerable gas in the tissues, but whether this was introduced at the time of his injury or was the result of a gas infection was never determined. Tetanus antitoxin and gas serum were given. Débridement was done. The hand was treated immediately with x-rays, twice daily for the succeeding two days, and once on the third post-operative day. Temperature remained normal after

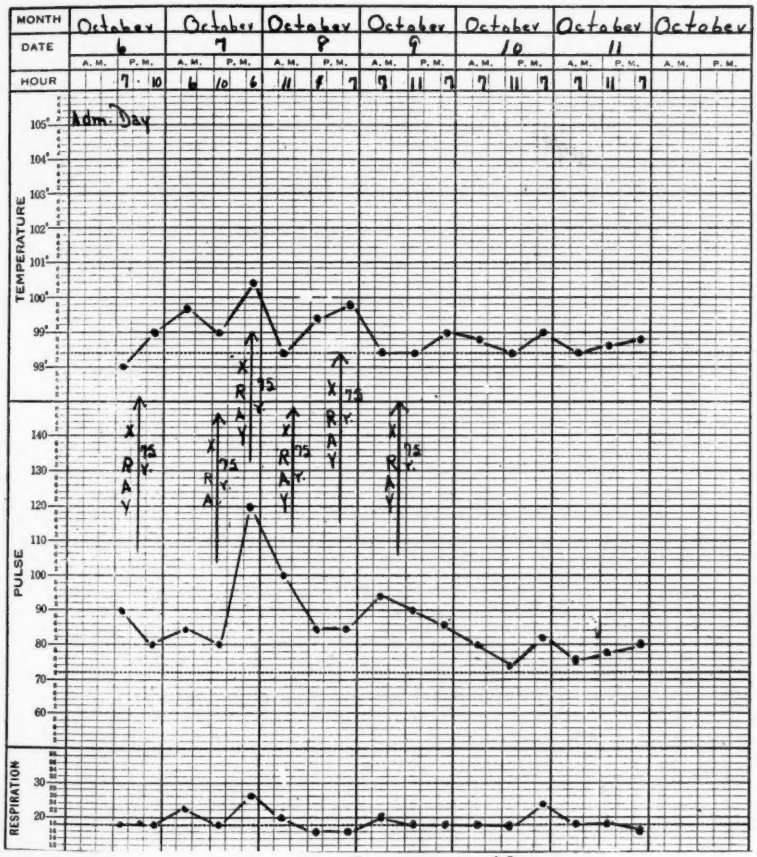


Fig. 9. Case 1: Severe hand injury treated prophylactically with x-rays.

that time. The patient was dismissed on the tenth postoperative day.

Comment: This patient was treated without delay and, although he had an extremely severe wound with evidence of infection and fever, the temperature dropped promptly to normal and the soft tissues repaired rapidly. Osteomyelitis did not develop, as commonly happens with this injury. The patient received antitetanus and anti-gas serum, but no sulfanilamide.

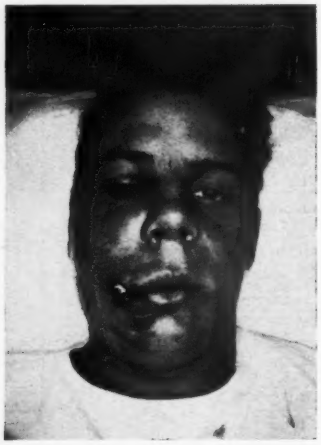


Fig. 10. Case 2: Second day after injury, showing condition of the right side of the face and the wound of entrance at the right angle of the mouth.

Whether this case is listed as a gas gangrene with recovery or in the group of cases in which x-rays were used as a prophylactic measure seems immaterial; the value of the treatment in hastening a prompt recovery without any mutilating surgery is the important thing and this was appreciated by the clinicians, who felt that the period of hospitalization was shortened as a result of irradiation.

This is a typical case of severe injury with considerable gas in the tissues receiving such early x-ray treatment that it is impossible to state definitely whether or not a gas bacillus infection was present. The fever, though low, was accompanied by a disproportionately rapid pulse, which is often seen in a beginning gas infection. It is better, however, to be uncertain about the diagnosis and save the hand than to be certain about the diagnosis and lose the hand. The scientific accuracy in diagnosis demanded by a certain type of research worker who never treats a case of anything from one year to another does not always appeal to the practitioner who has the responsibility of treating the patient.

It will be noted that more than the usual number of treatments recommended for prophylaxis were given in this case. This was due to the fact that the evidence of infection was apparent. This patient is not listed among our gas gangrene cases, as no cultures were made and the gas in the tissues may have been the result of the injury.

CASE 2: F. E. B., white male, age 18, was accidentally shot through the right cheek while hunting. The bullet (.22 caliber) entered about one inch above the outer angle of the mouth, lacerated the inner mucosa of the cheek for about two inches, struck the first upper molar, and the main fragment lodged in the neck.

Physical examination showed the right cheek to be swollen and edematous. There was a small pencil-size perforation leading into the cheek about one inch above and lateral to the right corner of the mouth. The mucosa of the right cheek was lacerated and bleeding.

The x-ray films of the facial bones showed two fair-sized metallic fragments, the smaller in the right nasal-antral wall and the larger posteriorly inside the ramus of the jaw near the great vessels, on a level with the first cervical vertebra. There were several fragments of metal scattered along the course of the bullet.

The laboratory findings were as follows: hemoglobin 86 per cent, red cells 4,280,000, white cells 7,400, mononuclears 1 per cent, lymphocytes 5 per cent, neutrophils 94 per cent, staff cells 4 per cent, segmented cells 92 per cent, urine negative.

The patient was given 10,000 units of perfringens antitoxin, 500 units tetanus antitoxin, and prophylactic irradiation to the face for gas gangrene. He received five x-ray treatments in four days and left the hospital on the eleventh day in good condition. The bullet fragments were not removed.

Other treatments were sodium perborate irrigations, hot boric compresses to the right eye, oil of cloves to the gum, and empirin for pain. No sulfonamides were used.

Comment: This patient left the hospital on the eleventh day after the injury

and had no further trouble. To reach all the damaged tissues in a wound like this with any local antiseptic is obviously impossible; the x-ray, however, is an ideal agent and if it proves to be consistently effective no logical objection to its use under such circumstances can be offered. It deserves an extended and impartial trial in traumatic surgical clinics under conditions favorable to its use, that is without the simultaneous use of any agent which is incompatible, such as the sulfonamides or the use of radiopaque dressings.

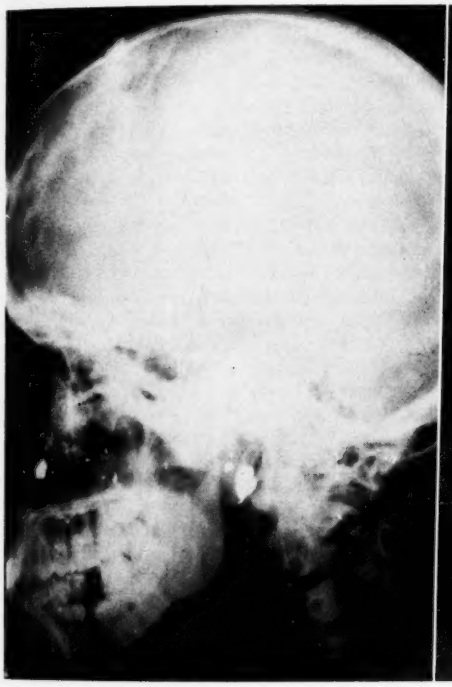


Fig. 11. Case 2: This lateral view of the facial bones shows the wide distribution of bullet fragments with the main fragment lying near the great vessels of the neck. Obviously it would be impossible to reach all the damaged tissues with any local antiseptic.

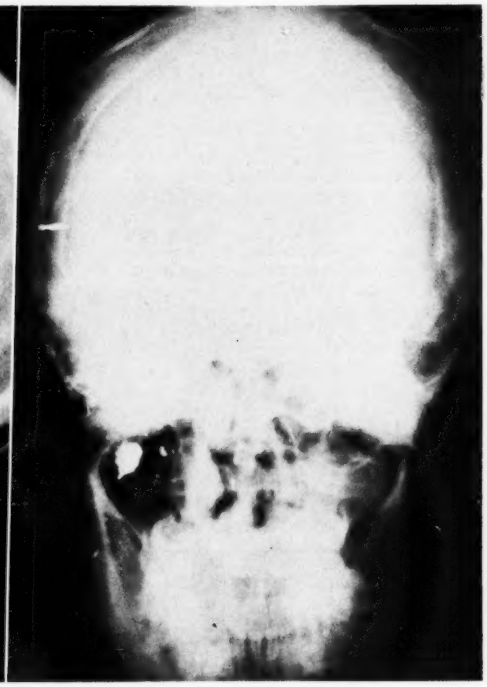


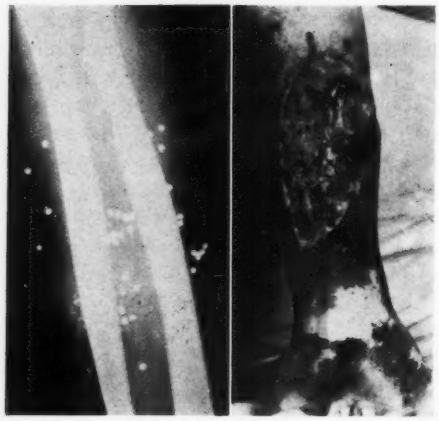
Fig. 12. Case 2: The posterior-anterior view shows the wide distribution of the bullet fragments from the nasal septum in the mid-line to the outer wall of the antra. The main fragment lies somewhat higher than its point of entrance at the angle of the mouth.

SULFANILAMIDE

For many years we believed that all the usual therapeutic measures could be used in conjunction with x-ray therapy but in 1938 we stated in a paper presented before the Radiological Society of North America that it was quite evident from our experience that sulfanilamide and x-ray therapy could not be used simultaneously with good effect (5). This observation was restated in the *United States Naval Medical Bulletin* (6) and the *Victor News* (7). Others have also made the same observations both clinically (8) and experimentally (9).

Until more is known about the interaction of these two agents they should not be combined. Furthermore, statistics and other data relative to the use of x-ray therapy in infections, when derived from cases in which sulfanilamide has been given at the same time, are not reliable and should not be quoted as proof of the inefficiency either of the x-ray or the drug.

In view of the importance of the present quest for an effective method of prevention of wound infections five cases are presented



Figs. 13 and 14. Case 3: Severe gunshot wound of arm. In such an injury it is difficult to understand how one expects to reach all the infected tissues by the local application of an antiseptic or how these tissues can be reached through the blood stream when some small areas are entirely cut off from their blood supply. The x-ray on the other hand has no trouble in reaching all the involved areas. The photograph on the right was taken four days after irradiation was begun. This case is presented through the courtesy of Dr. J. A. Muggly of Madison, South Dakota.

in detail. Cases 1 and 2, recorded above, are injuries of the type usually complicated by severe infection; both patients received prompt prophylactic x-ray irradiation and no sulfonamides; no infection occurred in either case. In Case 3 sulfanilamide was used in the wound and given by mouth. In spite of this, gas gangrene infection developed and was making considerable progress until the chemical was stopped and x-ray therapy started, after which prompt improvement occurred. The fourth patient received only sulfanilamide in the wound; gas gangrene developed and death occurred on the fifth day. This patient received no x-ray therapy. In Case 5 x-rays and sulfanilamide were used simultaneously, and the young patient lost both arms in spite of early and adequate x-ray dosage. Other cases in our experience have also shown a tendency to progressive gangrenous changes while receiving x-ray treatment when sulfanilamide or its early derivatives were being administered. Until more is known about combining these two agents in a therapeutic effort we do not expect to use them together. Patients who have been receiving sulfonamides are not treated with x-ray in our institutions until a twelve- to twenty-four-hour period has elapsed.

CASE 3: T. M., white male, age 17, was riding on a mower carrying a 410 gauge gun. The gun accidentally discharged and his arm, which was over the end of the barrel, was badly mangled and burned. Bleeding was controlled and he was immediately taken to a hospital.

On examination, his temperature was 98.2°, pulse 88, respirations 20. His expression indicated pain and shock. His abdomen was rigid, with tenderness on the right side, particularly in the lower right quadrant. The anterior surface of the right forearm was badly mangled, from the proximal to the distal third. The flexor tendons were exposed, and some were shot through. The ulnar artery was completely severed. Roentgen examination showed no bone involvement.

The wound was cleansed as well as possible, the ulnar artery was ligated, and the patient was given a prophylactic dose of tetanus and gas gangrene antitoxin. Sulfanilamide powder was placed in the wound, and sulfanilamide was also given by mouth, 90 gr. daily. The white cell count was 12,500 with 72 per cent neutrophils and 28 per cent lymphocytes; the red count was 4,610,000 with 100 per cent hemoglobin. Urinalysis was negative.

Convalescence was satisfactory until the fourth day after the accident, when the temperature rose to 101° and the pulse rate jumped from 70 to 100; respirations were 20. The wound had a foul characteristic odor; the forearm was beginning to swell. Smears from the wound at this time showed numerous *Cl. welchii*. The radiologist in consultation advised that sulfanilamide and serum be discontinued and x-ray therapy instituted.

The patient received three minutes irradiation over the upper arm and axilla and three minutes over the forearm, with two different exposures. Packs of 1:4000 potassium permanganate were used. The next morning the temperature was 99.4 but the pulse remained 100. Six treatments of three minutes each were given, and a final treatment of one minute.

The wound healed rapidly and convalescence was uneventful. Figure 14 shows the forearm four days after x-ray treatments were started.

Comment: This patient developed a serious gas gangrene infection in spite of the use of serum, sulfanilamide locally, and sulfanilamide by mouth, but responded promptly to x-ray therapy when the former measures, which failed to prevent or to control the progress of the gas gangrene, were discontinued.

CASE 4: A. W. F., colored male, age 58, was admitted to the hospital at 7:00 P.M., Sept. 25, 1940, with multiple injuries sustained when he was hit by an automobile shortly before admission.

The most severe of the injuries was a compound fracture of the left leg, the x-ray report of which was as follows: "Transverse fracture of the left tibia just above the junction of the upper with the middle third. Fragments are comminuted. Comminuted fracture of the fibula at the junction of the head and neck. Double fracture of the fibula just above the middle of the shaft. Fragment about 1 1/2 inches long." There was severe trauma to muscle and other soft tissues. A free end of bone protruded for a distance of 6 inches. The wound was filled with débris and grass.

Under local anesthesia the wound was thoroughly cleansed and irrigated with large amounts of sterile water. Bleeders were ligated, fracture was reduced, and sulfanilamide crystals were dispersed about the fracture fragments and throughout the wound. After approximation of the soft tissues and skin edges, the leg was immobilized in a plaster cast, which was split on the anterior surface to allow for swelling. Films taken after application of the cast showed the fragments in good position and alignment.

The patient was then given "combined tetanus serum" (type and amount not indicated on record), caffeine, sodium benzoate, and morphine 1/2 gr. His blood pressure at that time was 60/0. At 12:30 A.M. he was given 1,000 c.c. of normal saline with 10 per cent glucose and 8 units of histaminase. This was repeated at 10 A.M. the following day; the blood pressure was 76/50. The patient had a chill at 11:00 A.M. but the highest temperature recorded for the day was 99; pulse 120. He complained continually of severe pain in the leg and the abdomen became distended.

Cultures were taken on the third day (Sept. 27), and the laboratory report was "gas bacillus of the *B. welchii* type." Death occurred at 11:00 P.M. on Sept. 28. The temperature immediately before was 99°, pulse 110, respiration 30. No sulfanilamide was given by mouth or by hypodermic injection; it was used only in the wound, while in Case 3 it was used both orally and in the wound; in each instance it failed to prevent the onset of the disease.

Comment: This patient received sulfanilamide in the wound at admission and it was relied upon to prevent gas gangrene. In spite of this, gas gangrene developed and death occurred on the third hospital day. Serum was given only at admission, and no x-ray treatments were given at any time to prevent the development of a gas gangrene infection. This patient died in a hospital ten years after a sure method of treating gas gangrene was advocated in this area! Experience in this vicinity with sulfanilamide has not been such as to warrant its use in preference to x-rays in the prevention or treatment of gas gangrene. A brief survey of the literature would indicate that others have had similar experiences elsewhere (10).

CASE 5: A white boy, age 12, fell from a cherry tree forty-eight hours prior to admission, sustaining a fracture of the left ulna and radius above the wrist with protrusion of bony fragments through the skin. There was a simple fracture of the right ulna through the olecranon process and of the right radius through its neck, and also a simple fracture near the lower end of the radius, with all fragments in good position. The local doctor gave anti-tetanus serum, cleansed the open wound of the left forearm, and attempted reduction of the fractures. Splints were applied to the right arm and plaster to the left arm. On the following day increasing pain and rise in the temperature were noted. Sulfanilamide was given and continued for thirty-six hours prior to hospital entry.

Examination on admission showed lack of sensation and motor ability in the left arm below the elbow. The tissues were swollen and crepitant, and a foul sanguineous exudate oozed from the wound. The hand was black and there was loss of sensory and motor ability below the wrist. Temperature at entry was 102.5°, pulse 120 to 140. Roentgen examination showed the fractures enumerated above and also gas in the soft tissues about the left wrist, extending up to the middle half of the forearm. No definite break in the skin of the right forearm or wrist was seen.

An x-ray treatment was immediately given over the entire left arm up to and including the shoulder, 75 r, 100 kv., no filter, 50 cm. distance. During the following day, two doses of 50 r each were given. On that evening it was noted that gas was developing in the right hand and forearm (an extension of the disease to the other arm). To this area 75 r were delivered immediately following discovery, and 60 r were delivered over a laceration on the scalp as a prophylactic measure. During the next three days 50 r were delivered twice daily over the right forearm, hand, and shoulder, and once daily over the left arm. For three more days 50 r were given once daily over both arms. From June 16 to June 23 a total of 525 r units were delivered over both arms.

From June 16 to June 19 the patient received 10 grains of prontylin every four hours and from June 16 to June 22 10 gr. of sulfanilamide three times a day. His temperature and pulse gradually returned to normal. On July 5, his temperature varied from 100 to 101, pulse 90 to 110. At this time the right arm was black up to the elbow and the left arm was gangrenous to the wrist. The left hand was amputated above the wrist and the right above the elbow. The temperature continued to run between 99 and

100 during the following week, and gradually subsided to normal after about two weeks.

Comment: We believe the tragic failure to control the gas infection in this case was due to the simultaneous use of the x-ray and chemotherapy. The failure of these two agents to work well together became evident to us early in 1938 through our inability to control some simple infections of other types. Later a survey of all the infections treated at Creighton Memorial St. Joseph Hospital during 1938 showed 31 per cent mortality in cases treated with x-ray and sulfanilamide, and only 16 per cent mortality in cases treated with x-rays alone, thus supporting our clinical impression statistically.

SUMMARY OF CASES

Cases 1, 2, and 3 are representative cases in which a satisfactory débridement or the use of local antiseptics is not practical. Obviously these difficulties are of no consequence if prophylactic irradiation is used, since the x-rays easily penetrate all cells and fluids in the involved area without adding any extra hazard to the care of the patient. We have every reason to believe that x-rays are anti-infective for recent wounds. If this be true, what other agent can be administered to all the involved tissues with as little effort and greater certainty of beneficial effect? An impartial clinical trial in civilian hospitals on an extensive scale seems indicated, especially in view of the present program for national defense.

In Cases 1 and 2 no chemicals were employed. X-ray alone was used and both patients left the hospital in ten days without any infection or other complications.

Case 3 shows the inefficiency of both local and oral chemotherapy. Gas gangrene developed after the use of the chemicals and recovery followed x-ray therapy. Irradiation was begun only after serum and chemotherapy were discontinued.

Case 4 illustrates the inefficiency of the local use of chemotherapy alone when extensive damage to the tissues is present. The patient developed gas gangrene and died. No x-ray therapy was used. Case 5 shows a most unfortunate outcome when the two methods were combined.

PLEA FOR CASE REPORTS

The whole matter of acceptance of x-ray therapy for gas gangrene even by its most severe critics has now reduced itself to the question of correctness of the diagnosis in the cases treated. Previously when a series of gas bacillus infections were reported, with a mortality of 50 per cent or higher, no questions as to the diagnosis were raised. When, however, the mortality dropped under x-ray therapy, as shown in Figure 1, the true character of the cases being treated was questioned, which is as it should be. The importance of accuracy of diagnosis must be kept in mind in reporting these cases. All the clinical and technical data should be given in detail, particularly the criteria of diagnosis, case by case; also whether or not serum or any of the sulfonamides was used either for prevention or therapy, and, if so, the dosage, time, and manner of administration, and the impression obtained of their effect.

It is urged that treated cases be reported as early as possible; also that cases in which prophylactic irradiation is given in gunshot wounds, compound fractures, etc., be placed on record. Let us strengthen our base line in the literature for comparison with other methods of prevention and treatment of wound infections. A report may be the means of saving an arm or a leg. There are many who have never heard of the x-ray as a means of prevention or treatment of gas gangrene, and still others who insist that there is not yet a sufficient number of cases in the literature to establish its true status. More reports will assist in solving these problems.

ACUTE PERITONITIS AND GAS GANGRENE

The probable similarity in etiology of gas gangrene and acute spreading peritonitis (11–17) suggests that the x-ray treatment of the latter disease might be as successful as has been the x-ray treatment of gas gangrene. In our hands the

response of patients with acute spreading peritonitis has been as prompt and convincing as it has been in gas gangrene.

SUMMARY

Many facts of interest and some of importance have developed directly and indirectly from a twelve-year study of the x-ray treatment of gas gangrene:

Directly: 1. The x-ray provides a certain and definite means of prevention and treatment of gas gangrene.

2. The x-ray has made the use of serum unnecessary as a means of preventing and treating gas gangrene. Irradiation is effective after serum fails.

3. The cases analyzed suggest that the use of serum may even be harmful to the diabetic who develops a gas infection. This finding raises the question whether or not aged patients can withstand any type of serum without injury.

4. The x-ray has been used successfully for the prevention of other varieties of infection after recent injuries as well as gas gangrene.

5. The x-ray has removed gas gangrene from the class of acute diseases having a high mortality and morbidity, in which experimental therapeutic measures are justifiable.

6. Finally, the x-ray has completely eliminated the necessity of extensive surgery as a means of treating gas gangrene during its acute invasive stage. Any surgery indicated by the initial injury or disease should be performed, but no surgery directed toward the treatment of the gas gangrene is required, with the occasional exception of a few incisions to relieve local tension caused by deep gas pockets or collected serum. Amputation and extensive débridement are now obsolete procedures in the toxic stage of the disease and have been practically eliminated after the disease has subsided, because they are seldom necessary. They should *never* be necessary if treatment is started early and is properly given.

Indirectly: 1. This study has been a factor in the promotion of the general use of x-ray therapy for inflammatory disease at the bedside, with an apparatus of adequate kilovoltage.

2. Due to the similarity of organisms involved in gas gangrene and acute spreading peritonitis, the x-ray has been used in the latter disease with excellent results, and further investigation of this procedure is indicated.

3. It has been proved quite conclusively that the x-ray and sulfanilamide should not be used at the same time in acute inflammatory processes. Prior to the use of the sulfonamides the x-ray was able to halt the progress of the gangrene-forming infections in practically all instances, but when the two agents are combined the destruction of tissue continues; in fact it seems to be accelerated.

4. The curative action of the x-ray in gas gangrene establishes beyond any doubt the fact that the x-ray is of value in treating infections, since the gas infections are uniformly resistant to other treatments but respond consistently to x-ray therapy.

5. The antitoxic effect of the x-ray in acute infections is amply demonstrated in treating gas gangrene, acute spreading peritonitis, surgical mumps, erysipelas, and other toxic acute infections. This general reaction as well as the favorable local effect was evident to many clinicians years before gas gangrene was treated with x-rays, but as other measures at times had the same effect it was difficult to establish the value of x-rays in this regard. As the late Willis Manges pointed out to this writer, their action in gas gangrene is unparalleled by any other measure, and this has placed the value of the x-ray in treating certain acute toxic infections well above any reasonable criticism.

This antitoxic effect is apparently nonspecific, resembling the non-specific effect in preventing peritonitis after colon and rectal surgery, an action first reported by the Ford Hospital group (16).

CONCLUSIONS

The x-ray should be used early in gas bacillus infection but will cure many cases

in the late stages with little or no danger to the patient and at the same time provide for the maximum of tissue recovery. It will also prevent the disease. If a means of treatment is discovered which will do more, it should be used. In the meantime, x-ray therapy is indicated in man; experimental measures should be confined to the usual well recognized experimental channels.

Sulfanilamide and its early derivatives are definitely incompatible with x-ray therapy. We know nothing about the later sulfonamides but will not give x-ray therapy where they are used at this time. If they must be used they should be used alone until more study of the problem has been completed.

No harm has ever come from x-ray therapy alone as used in the treatment of acute fulminating infections.

There is a rapidly accumulating literature to support the data presented in this communication. To assist in clarifying any points of controversy which may arise in this study all are urged to report their cases in detail in the literature.

Note: To the many physicians who have contributed to this study for the past several years the writer (J. F. K.) is sincerely grateful. Without their aid this work would not have been possible. Through their generous co-operation, results equivalent to fifty or more years of study and progress in the treatment of gas gangrene have been compressed into ten years, and all the terror has been taken out of gas gangrene. In fact it has been made an unnecessary disease.

816 Medical Arts Building, Omaha, Nebraska

REFERENCES

1. KELLY, JAMES F.: The X-ray as an Aid in the Treatment of Gas Gangrene. Radiology **20:** 296–304, April 1933.
2. COLEMAN, E. P., AND BENNETT, D. A.: Personal Experiences with Gas Bacillus Infection. Am. J. Surg. **63:** 77–80, January 1939.
3. HUBENY, M. J., AND MCNATTIN, R. F.: X-ray Therapy: Evaluation of Its Use in Treatment of Diseases of Non-malignant Neoplastic Nature. Urol. & Cutan. Rev. **42:** 436–441, June 1938.
4. THOMSON, J. E. M.: The Ten Commandments for the Treatment of Compound Fractures. J. A. M. A. **115:** 1855–1860, Nov. 30, 1940.
5. KELLY, J. F., AND DOWELL, D. A.: Roentgen Treatment of Acute Peritonitis and Other Infections with Mobile X-ray Apparatus. Radiology **32:** 675–692, June 1939.
6. KELLY, J. F., AND DOWELL, D. A.: Roentgen Treatment of Acute Infections. U. S. Nav. M. Bull. **37:** 600–610, October 1939.
7. KELLY, J. F.: Sulfanilamide. Victor News, General Electric X-ray Corp., December 1939.
8. MARKS, M. B.: Hypersensitivity to Sulfanilamide Following Roentgen Therapy. J. Pediat. **16:** 503–506, April 1940.
9. FLOCKS, R., FELLOWES, O. N., AND KERR, H. D.: Combined Action of Roentgen Rays and Sulfanilamide on Staphylococcus aureus. Am. J. Roentgenol. **44:** 115–116, July 1940.
10. MACY, H. B.: Gas Gangrene: Report of a Case. Proc. Staff Meet. Mayo Clin. **14:** 180–183, March 22, 1939.
11. WELCH, W. H., AND FLEXNER, S.: Observations Concerning the Bacillus aerogenes capsulatus. J. Exper. Med. **1:** 5–45, January 1896.
12. WILLIAMS, B. W.: The Importance of Toxemia Due to Anaerobic Organisms in Intestinal Obstruction and Peritonitis. Brit. J. Surg. **22:** 295–322, October 1926.
13. BOWER, J. O.: Spreading Peritonitis Complicating Acute Perforative Appendicitis. J. A. M. A. **112:** 11–17, Jan. 7, 1939.
14. MCCLURE, R. D., AND ALTEMEIER, W. A.: Acute Perforated Appendicitis with Peritonitis. Ann. Surg. **105:** 800–814, May 1937.
15. ALTEMEIER, W. A.: Bacterial Flora of Acute Perforated Appendicitis with Peritonitis. Ann. Surg. **107:** 517–528, April 1938.
16. ALTEMEIER, W. A., AND JONES, H. C.: Experimental Peritonitis: Its Prevention by X-ray Irradiation. J. A. M. A. **114:** 27–29, Jan. 6, 1940.
17. PASTERNACK, J. G., AND BENGTSON, I. A.: Experimental Pathology and Pathologic Histology Produced by the Toxin of Vibrion septique in Animals. National Institute of Health, Bulletin No. 168, 1936.

DISCUSSION

Robert J. May, M.D. (Cleveland, Ohio): Our experience in the x-ray treatment of gas gangrene has been limited to 8 patients, 2 of whom died. One of the 2 was a diabetic who had had an infected foot for at least two weeks before admission to the hospital, with a superimposed gas infection. She was in coma when brought to the hospital. She had one x-ray treatment and died well within twenty-four hours after admission. The other death was that of a patient who had fractures of a number of the ribs, lacerations about the face and chest, and possibly a fractured skull. As a result of these injuries he lost a great deal of blood. The gas gangrene was under control at the time of his death, which we believe was due to the severity of the injuries and hemorrhage.

Of our 6 patients who recovered, all received some treatment in addition to x-ray irradiation. All were given serum, and possibly all received sulfanilamide. In several cases the tissues were incised, and in 2 amputation was done. Our surgeons will not consider omitting any of the therapeutic procedures which have been used in successfully treated cases.

We have had no experience with what Dr. Kelly has called prophylactic x-ray therapy in the severely traumatized patient, but we believe that this should be tried, as x-ray therapy should be tried in many other forms of infection.

Dr. Kelly's paper is complete, concise, and convincing, and he is to be congratulated on his presentation.

Edgar P. McNamee, M.D. (Cleveland, Ohio): Dr. Kelly has initiated and popularized the use of x-ray therapy for gas gangrene. His statistics show that much better results are obtained by this means than by any other method or all other methods combined. Our experience at St. Alexis Hospital is in accord with his.

Dr. Kelly uses the term prophylactic to describe the treatment of a patient before gas gangrene can be recognized clinically. This term should not be used, since it is impossible by x-ray therapy applied to the patient or causative organism to prevent gas gangrene. X-ray therapy is potent only when the gas gangrene organism has entered the tissues and has produced a reaction in the patient. X-ray therapy, given at this early stage, is actual treatment and is not a prophylactic measure. I agree with Dr. Kelly that irradiation should be given early, as soon as gas gangrene is diagnosed or even suspected.

Dr. Kelly's studies indicate that the results obtained by x-ray therapy combined with sulfanilamide therapy are not as good as those with x-ray therapy alone. This is an important point and should be given full consideration by all those concerned in the treatment of gas gangrene. No therapeutic agent which will destroy white blood cells or reduce their number should be used concurrently with x-ray therapy in the treatment of gas gangrene.

Abraham Strauss, M.D. (Cleveland, Ohio): I should like to ask Dr. Kelly if his preference for radiation over sulfanilamide in peritonitis, which he barely mentioned, would apply to *B. coli* peritonitis after an appendectomy, and if he would use it routinely.

Dr. Cooper: I should like to ask Dr. Kelly about dosage.

James F. Kelly, M.D. (*closing*): Dr. May mentioned a diabetic patient. It is difficult to state what will eventually be done about this group of patients. Their primary disease is so difficult to manage and the mortality has been so high that we are not certain as to how much good can really be accomplished. The omission of serum and the use of x-ray alone may be a distinct help.

The omission of serum, may, however, have some bearing in malpractice suits and for this reason everyone is requested to report his cases in the literature in detail so as to establish the fact that serum may be omitted with benefit to the patient. Our present figures go back several years and should be of value in this respect. They suggest that serum is harmful in the presence of diabetes.

Dr. McNamee objects to the term prophylaxis. What we have called prophylactic irradiation is not really a vaccination; I will grant that. But if it prevents the infection from becoming established, as it does, then it is prophylaxis in the same sense that cleansing the wound is prophylaxis. These two measures work very well together. If it is possible to abort an early infection, as has been done many times with the use of x-rays, we should not question the value of x-rays in prevention, for surely they should be able to prevent any infection which they can abort. There are many fathers and mothers who would cheerfully pay for one x-ray treatment each day for three days to prevent an infection in a compound fracture, since osteomyelitis as well as gas gangrene is apparently prevented.

The question regarding the effect of the x-ray in colon bacillus peritonitis cannot be answered at this time. We have treated many types of peritonitis, but not with adequate bacterial studies to enable us to say just what effect the x-rays have on any particular organism. We believe the x-ray has a beneficial effect in the treatment of any infection with a gas-forming organism, but we would not care to give any definite answer relative to its action on the colon bacillus. We treat peritonitis whenever we get a chance, unless the patient is saturated with one of the sulfonamides. If no sulfonamides have been given for twelve hours or more we use x-rays, but do not do as well either in regard to mortality or morbidity as we do if sulfonamides are omitted. In four years at Creighton Memorial St. Joseph's hospital we have treated 66 cases of peritonitis with the x-rays, with 12 deaths. During the same period of time in the same hospital there have been 75 cases treated by all other methods, with 46 dead. In other words, the records show a mortality of 18.1 per cent with x-ray therapy against a mortality of 61.3 per cent with other measures. Peritonitis, however, is a very irregular disease, due to many organisms, and it will be many years before we can draw the sharp conclusions regarding it that we can now draw on the x-ray treatment of gas gangrene.

In regard to dosage. For treatment, we give 150 r units per day in two doses of 75 r or three doses of 50 r to the entire abdomen or the area we believe infected. For prophylaxis, we give 75 r daily in one dose. The kilovoltage varies from 90 to 130, depending on the thickness of the part. Filtration increases with kilovoltage.

Roentgen Radiation in Experimental Clostridium welchii Infection (Gas Gangrene) in Dogs: Preliminary Report

ANDREW H. DOWDY, M.D., and ROBERT L. SEWELL, M.D.

Rochester, N. Y.

IN VIEW OF THE increasing military significance of "gas bacillus" infection, a brief preliminary report of the experimental methods that we have employed in an investigation of the effects of roentgen radiation upon the infection with *Cl. welchii* in dogs during the last two years may prove of value and be encouraging to other workers in this field. There has been a great deal of discussion about the possible effectiveness of roentgen radiation in the treatment of clinical cases of gas gangrene (*Cl. welchii*). In experimental animals, as well as in man, there is some variation in individual susceptibility to the disease, irrespective of the virulence of the infecting organisms. Experimental work with the disease in mice, guinea-pigs, rabbits, and other animals has, in general, been unsuccessful, chiefly because the course and outcome have been so unpredictable.

After considerable unsatisfactory preliminary work with small animals, we have been successful in establishing a fairly constant syndrome in dogs following the intramuscular injection of a twenty-hour unwashed subculture of *Cl. welchii*. This has made possible a preliminary test of the effects of radiation upon the disease.

There are a number of pathogenic gas-producing organisms which may be the etiological factor in the production of clinical gas gangrene in man. These may occur in pure culture but most frequently are found along with pyogenic organisms, in various combinations. The organism most frequently present in clinical gas gangrene is *Cl. welchii*. Clinically it must be evident that all gas-producing organisms are not pathogenic. Experimentally, gas gangrene can be produced with most of the pathogenic forms.

Since September 1940, the disease has been consistently produced in 66 dogs. The pathological process is not unlike the infection occurring in man, and is much more predictable in extent and toxicity than that seen in small animals. Sixteen of the 66 dogs were used for biological standardization. The remaining 50 were used as test animals, 25 serving as controls, and 25 receiving roentgen radiation.

Gas was usually observed deep in the muscle about six hours after inoculation, followed by a progressive development of edema, redness, and exquisite tenderness of the part. In many cases the infection extended to the subcutaneous tissues. The skin then became very edematous and bluish black. If the animals survived beyond thirty-six hours, the advancing tissue necrosis caused disintegration of the skin and a draining sinus formed. With drainage thus spontaneously established, recovery ensued in approximately 95 per cent of these animals (treated or untreated).

The dogs were all normal, active adults in good physical condition. Immunization against distemper was not carried out because of the brevity of each individual experiment. The animals were matched in pairs as nearly as possible with regard to weight, age, and general vigor. In those instances where there was some variation, the older, the smaller, or the less vigorous animals were irradiated and the potentially stronger animals were used as controls, thus throwing the burden of proof upon the therapeutic agent.

To circumvent variations in the organism from culture to culture, and changes in virulence with age, the entire series of 66 dogs was inoculated with injections from a

[1] From the Departments of Radiology and Surgery, University of Rochester, School of Medicine and Dentistry, and the Strong Memorial Hospital, Rochester. Aided in part by a grant from the National Research Council. Accepted for publication in May 1941.

single pure culture of the organisms which had rested undisturbed in a deep meat tube in an icebox for five months prior to the beginning of the experiment. Each inoculum was a twenty-hour, unwashed culture taken from the master tube. This was mixed with a tenth part of 1:1,000 adrenalin immediately before inoculation. Each of the 4 dogs in each weekly experiment was given a dose of the same size from the same subculture. All injections were made intramuscularly in the thigh, the needle being run in until the femur was reached, and the inoculum then injected into the surrounding muscle.

Weight alone was found to be a poor basis for establishing the lethal dose. The lethal effect is apparently due to extension of the local lesion through diffusion of the gas and infection in the tissues, rather than to a primary systemic effect. This is exemplified by the fact that 0.2 c.c. will consistently cause death in guinea-pigs, while only 6 times this amount is necessary to kill a dog weighing some 30 times as much as the smaller animal; 1.2 c.c. will kill small dogs fairly uniformly, while 1.35 c.c. will kill one over twice as large.

The dose was initially standardized by using 8 dogs, and the minimal lethal dose was set around 1.25 c.c. Two subsequent standardizations at intervals of sixty days were made, 4 dogs being used each time. These animals were given 0.9, 1.1, 1.3, and 1.5 c.c., respectively, and only the 2 receiving the smaller doses survived. It is easily proved that *Cl. welchii* infections produce a relative immunity. In order to ascertain the effect of irradiation in such animals with previous exposure, the surviving dogs were reinjected with doses varying from 2.0 to 5.0 c.c. of the inoculum. In this group there were 20 dogs, including some of those used for the biological standardization: 10 were irradiated, 10 serving as controls. Most of the animals lived.

Radiation Technic: The technic of treatment has of necessity varied in this pre-

	25 IRRADIATED ANIMALS			25 CONTROL ANIMALS		
	No. Dogs	No. Survivals	% Survivals	No. Dogs	No. Survivals	% Survivals
TOTAL ANIMALS	25	9	36	25	5	20
RECEIVED 1.25 C.C. OR MORE OF INOCULUM.	16	5	31.3	16	2	12.5
RECEIVED LESS THAN 1.25 C.C. OF INOCULUM.	9	4	44.4	9	3	33.3
120 KVP, 3 MM. AL FILTRATION, HALF VALUE 3.55 MM. AL	17	7	41			
200 KVP, 0.5 MM. CU, HALF VALUE 0.95 MM. CU	8	2	25			
TWO TREATMENTS DAILY.	13	5	38.5			
ONE TREATMENT DAILY.	12	4	33.3			
TREATED 4 HOURS OR LESS AFTER INJECTION.	21	8	38			
TREATED LATER THAN 4 HOURS AFTER INJECTION.	4	1	25			
RECEIVED MORPHINE.	13	4	30	13	4	30
NO MORPHINE.	12	5	41.6	12	1	8.3

Fig. 1. Results of irradiation of 25 dogs as compared with 25 unirradiated controls, irrespective of technical factors (first line). The subsequent divisions of the chart represent the results obtained from varying the technical factors.

liminary study. It was important to determine as best we could the optimum interval between the inoculation and the first treatment, the frequency of the treatment, the size of the individual dose, and the required kilovoltage. In the majority of instances the individual dose has been 100 r (measured in air). The portal has varied from 20 × 20 cm. to 20 × 30 cm., but has always been sufficiently large to include the involved area. This varied with the size of the dog, but in every instance it included the entire hind leg. Frequently it was difficult, at the first

SURVIVAL PERIOD OF ANIMALS SUCCUMBING TO DISEASE		
	NO. DEATHS	AVERAGE SURVIVAL PERIOD
IRRADIATED GROUP	16	45.4 HRS.
CONTROL GROUP	20	24.5 HRS.

Fig. 2.

treatment, to keep the animal sufficiently quiet. To obviate this, morphia (0.015 gm. morphine) was given three hours before irradiation, and a like amount was given to the controls. Figure 1 presents an analysis of the data obtained.

If dose, type, and frequency of treatment are disregarded, the survival of 36 per cent in the irradiated group as against a survival of 20 per cent in the control group is not impressive. If, however, the aforementioned factors are considered, the results assume a greater significance (Fig. 1). It is to be noted that of the 16 irradiated animals receiving 1.25 c.c. or more of the inoculum, 5, or 31 per cent, survived, as against only 12.5 per cent survival of the 16 controls receiving this amount. The use of 120 kv.p. with a half-value layer of 3.55 mm. Al gives a survival of 41 per cent as against 25 per cent for 200 kv.p. with a half-value layer of 0.95 mm. Cu.

Treatments initiated four hours or sooner after inoculation produced an appreciable increase in survival rate over treatment initiated later than four hours following inoculation. Of the 13 animals in the irradiated group which received morphine, there were 4 survivors. One animal in the irradiated group received 1.35 c.c. and one received 1.4 c.c. of the inoculum, whereas all 4 survivors in the control group having morphine received 1.2 c.c. of the inoculum (less than the usual lethal dose). This suggests that morphine does not affect the outcome. In the control group, there were 12 dogs which received only 1.2 c.c., with a survival of 4 animals, or 33.3 per cent. Figure 2 shows the average survival of the animals that died to be approximately twice as long in the irradiated group as in the control group.

The group of 20 survivors which, therefore, had some degree of immunity were reinjected. One animal died in the irradiated group, a 10 per cent mortality, while among the 10 dogs of the control group there were 3 deaths, or a mortality of 30 per cent.

With the completion of these preliminary experiments, it is evident that a standard type of reaction can be established, and it will now be possible to study the effects of different amounts of roentgen dosage administered at different intervals after injection; to partition the inoculum and study the *in vitro* and *in vivo* effects of radiation on the various parts of the inoculum; and to survey the effects of a series of sulfanilamide compounds alone and in combination with radiation.

SUMMARY AND CONCLUSIONS

1. A definite syndrome quite comparable to *Cl. welchii* disease in man has been produced in 66 dogs.

2. In a series of 50 dogs, irradiation of 25 has been shown to have some therapeutic effect in combatting *Cl. welchii* infection as compared with the 25 controls.

3. Preliminary studies on the effect of varying the factors of time, amount of treatment, size of dosage, and kilovoltage requirements are recorded.

260 Crittenden Boulevard, Rochester, N. Y.

Influence of the Emotions upon Esophageal Function: A Comparison of Esophagoscopic and Roentgenologic Findings[1]

WILLIAM B. FAULKNER, JR., M.D., F. H. RODENBAUGH, M.D., and JOHN R. O'NEILL, M.D.

San Francisco

THE MAJORITY of physicians and surgeons have been reluctant in accepting wholeheartedly the contention of the psychiatrists that emotions can so disturb organic function as to produce severe symptoms which are indistinguishable from those of definite organic disease. They all know, either from experience or otherwise, of patients who have been pronounced neurotic and so treated over long periods, and ultimately found to be victims of an undiagnosed ulcer, carcinoma, or other organic lesion. The danger of such a serious error justifies the skeptic scrutiny that has been given to these psychiatric theories.

If the psychiatrist's idea of functional disturbances is correct, we should expect some objective evidence of alteration in the "emotionally affected" organ, and an unmistakable relationship between the emotion in question and the effect produced. At first glance, the approach to the study of this functional problem seems beset with obstacles, because in most of the bodily organs it is not easy to prove or disprove an alliance between the emotional cause and the dysfunction.

This subject first claimed our attention some years ago during an esophagoscopic examination, in search of an organic lesion, in a patient who was exhibiting symptoms of esophageal dysfunction. We found a severe spasm of undetermined etiology, and then noticed that a chance statement of ours caused the spasm to disappear, while an opposite trend of conversation re-elicited it. It was difficult to believe that which we saw transpiring before our eyes, but the changes were unmistakable, and reversible. Spasm was brought about by the discussion of unpleasant subjects and the arousing of undesirable emotions, while its disappearance occurred when pleasant and "wished-for" situations were envisioned (1, 2).

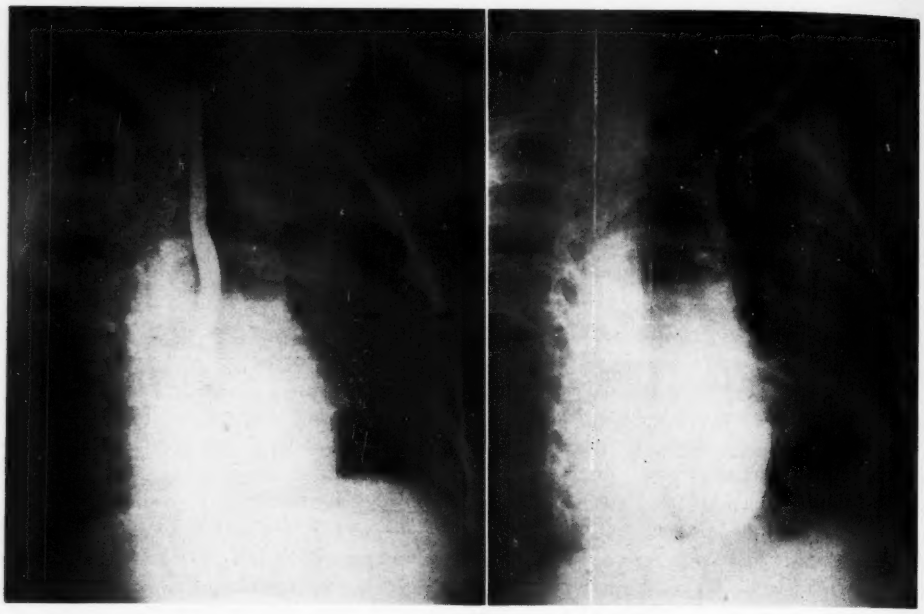
It was, of course, quite possible that this psychosomatic response was peculiar to this particular patient, and might be absent in all others, but our curiosity was awakened and we were anxious to settle the point if possible.

Up to the present time, on esophagoscopic examinations, we have found such objective psychosomatic changes in 25 patients. Thirteen of these cases have been reported (3), but our discussion of them was solely from the standpoint of esophagoscopy. The present paper considers these same emotional alterations and dysfunctions from the point of view of roentgenologic study and interpretation.

Every roentgenologist has occasionally observed fleeting, transient spasms of the esophagus during routine gastro-intestinal investigations; he also has a thorough acquaintance with the more permanent type of spasm called "cardiospasm." These observations are not in themselves new, but doubt does exist as to the causes and real significance of these variegated esophageal spasms.

Although the roentgenologist has assured himself that no organic lesion is present, he is at the same time quite aware that something has happened to disturb the normal esophageal action. Yet he does not mention these spastic changes in his reports, principally because he is unable to explain them. Are they brought on by the emotions? Can they be relieved by opposing emotions, as has been demonstrated by esophagoscopy, a procedure which in itself probably causes a cer-

[1] From the Thoracic Surgical and Roentgenological Departments of St. Mary's and Mary's Help Hospitals, San Francisco. Accepted for publication in November 1940.



Figs. 1 and 2. Case 1: Esophageal spasm. In the film on the right, made five minutes after the other, the main mass of barium has passed, but the walls of the esophagus are still faintly outlined.

tain amount of tension and apprehension? Can routine x-ray studies furnish as conclusive objective evidence of the relationship between the emotional stimulus and the ensuing spasm, or relaxation, as esophagoscopy? In an attempt to answer these questions, this investigation was undertaken.

(1) The first case that we wish to report is that of a woman, aged thirty, who was referred to us for esophageal study after having spent three years visiting the various departments of the clinic without obtaining appreciable relief. On fluoroscopy the picture was that of severe cardiospasm. When suggestions were made to arouse pleasant emotions, the barium instantly ran into the stomach, all signs of cardiospasm disappeared, and further immediate ingestion showed no esophageal spasm.

Being aware that this patient had had considerable family difficulty, we asked her if her husband had ever given her a black eye. Her answer was, "Yes, twice. But he better not try it again." She was then asked to imagine exactly how she felt when he struck her. The next spoonful of barium paste revealed a completely different esophageal picture from the one seen two minutes before. Now there was retention of all the paste, not directly above the diaphragm only, but throughout the entire length of the esophagus, in addition to a vigorous peristaltic movement with reverse peristalsis. Spasm persisted until another pleasant suggestion was introduced and the patient laughed. As the esophagus then emptied, we were led to suppose that if roentgen plates with barium were now made they would show no abnormality. But our supposition was erroneous. A new esophageal spasm was present at a different site.

We incorrectly predicted the esophageal status by overlooking the fact that spasms are controlled not only by the emotions which the physician intentionally arouses, but also by those which spring spontaneously from the patient's own thought processes. Very likely other emotions supplanted the pleasant ones that we had

previously called forth, hence the alteration and dysfunction (Figs. 1 and 2).

An esophagoscopic examination five weeks later confirmed the fluoroscopic and x-ray diagnosis of an emotionally controlled esophageal spasm. Through the esophagoscope we could see the alternating spasm and relaxation actually occurring in response to our suggestions.

(2) Our next patient was a door-to-door salesman who had been seen in many departments of the clinic. His original symptoms were dizziness, nervousness, and weakness; but ultimately he complained of nausea, vomiting, inability to swallow, and substernal pain. Since no pathology other than emotional spasm was encountered on esophagoscopic examination, a rational plan of living was outlined for him and his symptoms disappeared.

The barium fluoroscopic examination which was made two weeks later showed an immediate rapid emptying of the esophagus without apparent abnormality. We then asked him to imagine how he would feel if his salary commissions were reduced and his competition so increased as to jeopardize his chance of earning a living. While he was pondering this unpleasant and disturbing thought, a mouthful of barium paste was given, and a roentgen film made (Fig. 3).

We believe that the sudden alteration, deformity, and dysfunction of the esophagus in this case was brought about by the disturbing emotions which we aroused and the imaginary insecurity which we created, because previous to our suggestions the esophagus had emptied normally.

(3) A married woman, aged thirty-three, appeared at the clinic complaining of "a lump in the throat," difficulty in swallowing, and nausea after eating. Fluoroscopy with the thick barium paste showed that there was complete esophageal stasis, wide dilatation of the whole esophagus, and constrictions at irregularly scattered points throughout its full length. As these findings persisted, we asked the patient to imagine how she would feel if her social and economic problems were all solved. Immediately thereupon the esophagus emptied. At this point she was dismissed from the fluoroscopic room and allowed to sit alone for twenty minutes. Then more paste was given and a roentgenogram taken (Figs. 4 and 5).

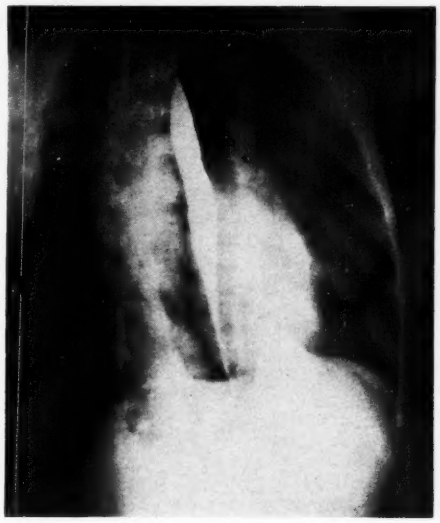
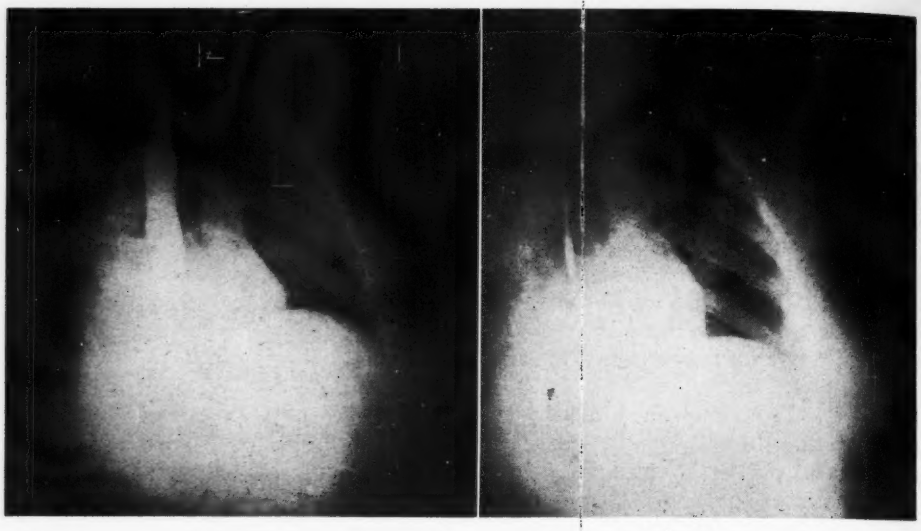


Fig. 3. Case 2: Esophageal spasm. Fluoroscopy immediately preceding showed no evidence of spasm.

Since the esophageal spasm was absent when the patient left the fluoroscopic room but was present on the film, we presumed that it was brought on by disturbing emotions which she herself aroused while meditating upon her difficulties. The emotional nature of the spasm was later substantiated on esophagoscopic examination. There was no organic esophageal lesion, and the symptoms disappeared when proper treatment was instituted.

(4) An especially interesting roentgen study was obtained in a single man of fifty-two who had complained of "pains in the chest and cramps in the bowels," and who had shown alternating emotional spasm and relaxation during esophagoscopy. After the esophagoscopic examination had been completed a plan of living was outlined for the man, but he refused even to listen to it. Instead he demanded a "bottle of medicine," "a certificate" in-



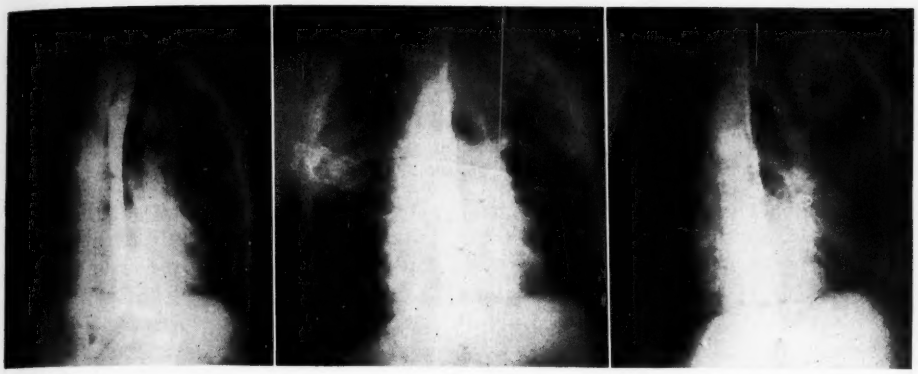
Figs. 4 and 5. Case 3: Irregular esophageal spasm involving the lower portion and showing dilatation above. Figure 5 (right), made seven minutes later, shows considerable barium still held in the esophagus. Dysfunction is evidenced by this delayed emptying, the normal emptying time being from four to nine seconds.

dicating that he was too sick to work, and an opportunity of receiving "financial sick relief." When these were not given he became sullen and disagreeable, and visited the clinic daily, restating his demands. This went on for five days, at the end of which time we temporarily appeased him by agreeing to do another fluoroscopic examination. This showed complete esophageal obstruction at the diaphragm, retention throughout the full length of the tube, and several localized constrictions. The esophageal responses to suggestions of an ordinarily pleasant environment were now about as stubborn as he himself had been in accepting our advice. There was very little emptying of the esophagus. When, however, we asked how he would feel if he were given a "sick certificate," the barium catapulted into the stomach. When we re-weighed our certificate decision and questioned the advisability of such action, he was again uncertain and sullen. A roentgenogram was now ordered with paste to be given just before taking the pictures (Figs. 6, 7, and 8).

In some of the young adults who complained of difficulty in swallowing, an additional finding was noted. The barium column suddenly came to a stop within one portion or another of the esophagus and there remained for as long as ten minutes, without showing an organic lesion, dilatation, spasm, or esophageal peristalsis. In fact, there was a complete absence of esophageal waves; when the patient attempted to swallow, the whole barium column was lifted *en masse* in the direction of the mouth but it did not move distal to the point of stoppage. Finally, after a prolonged stay, the opaque medium suddenly began to trickle forward, and passed into the stomach.

The other patients of "the esophagus group" that we examined roentgenologically were so much like those reported here that there is no purpose in presenting the detailed findings.

Attention should be called to the fact that if the roentgen examinations are made in the routine manner customarily employed in clinical practice, the emotional esophageal abnormalities may be missed even in patients who complain of esophageal symptoms. The abnormalities are dependent upon the patient's emotions at the moment and apparently are absent



Figs. 6–8. Case 4: The film on the left was made immediately after swallowing the paste. Note the esophageal spasm and deformity. The central film, made twelve minutes later, shows the esophagus well outlined by the retained barium. In the film on the right, made twenty-four minutes later, the spastic esophagus is seen still to retain considerable barium.

when the emotions producing them have been replaced by opposite feelings.

If no attempt is made to alter the patient's emotional stream, the esophagus may appear normal on fluoroscopy but show spasm and dysfunction on the film. Conversely, there may be a normal film despite abnormal fluoroscopic findings.

The mechanism of this seeming contradiction can be understood when one appreciates the lightning rapidity with which the emotions can change due to the patient's own pleasant and unpleasant thoughts, and thus alter the picture. On a basis of this work, it is conceivable that both the fluoroscopic and film examinations may occasionally fail to demonstrate the dysfunction. If symptoms persist and no x-ray abnormality has previously been noted, the examination should be repeated.

The roentgenologist is in a better position to evaluate the findings and the cause of the symptoms if he is apprised in advance of the patient's personal difficulties and emotional problems. Should any doubt at all exist, an esophagoscopic examination should be made without delay. In fact, a case of this type is but incompletely investigated if the esophagoscope has not been used, for a great responsibility rests upon the physician or surgeon who diagnoses a condition as functional and so treats it without first positively excluding the presence of stricture, ulcer, carcinoma, foreign body, or other possible cause of the symptoms.

It behooves the roentgenologist to call even the most transient spasms to the attention of the attending physician, since these are a clue to the emotional stability of the patient, and may be forerunners of more permanent "habit spasm" if left unattended.

CONCLUSIONS

1. Esophageal spasm and dysfunction can be produced by certain emotions.

2. By means of esophagoscopic and roentgenologic examinations these changes can often be observed while they are occurring, and the relationship between the emotional stimulus and the esophageal function can be conclusively established.

384 Post St., San Francisco, Calif.

REFERENCES

1. FAULKNER, WILLIAM B., JR.: Severe Esophageal Spasm: An Evaluation of Suggestion-Therapy as Determined by Means of the Esophagoscope. Psychosom. Med. **2:** 139–140, April 1940.

2. FAULKNER, WILLIAM B., JR.: Esophageal Spasm: Observation of Emotional Influences by Means of the Esophagoscope. Report of a Case. J. Nerv. Ment. Dis. **93:** 713–715, June 1941.

3. FAULKNER, WILLIAM B., JR.: Objective Esophageal Changes Due to Psychic Factors: An Esophagoscopic Study with Report of Thirteen Cases. Am. J. M. Sc. **200:** 796–803, December 1940.

Acute (Primary) Coccidioidomycosis: Roentgen Findings in a Group "Epidemic"

ROBERT A. POWERS, M.D., and DOROTHY J. STARKS, M.D.

Palo Alto, Calif.

AN "EPIDEMIC" OF acute (primary) coccidioidomycosis occurring among the fourteen members of a field trip to an endemic area recently afforded an excellent opportunity to observe the early roentgen findings in this newly recognized acute fungus infection.

Coccidioidal granuloma with its high mortality rate has been recognized since 1892, when Wernicke (1) discovered the double-contoured spherules in a patient's sputum, but it was not until 1937 that Dickson (2) first described the primary disease in the literature and furnished clinical and bacteriologic proof of its existence. ("Valley fever," "desert fever," "San Joaquin fever," or "the bumps" had long been familiar to San Joaquin Valley physicians.) A full description of clinical and bacteriological findings is contained in the papers of Dickson (2), Dickson and Gifford (3, 4), and Faber, Smith, and Dickson (5).

'Valley fever" patients are ill with an acute respiratory infection for from three to six weeks and most recover without complications. A permanent and effective immunity appears to be set up and second attacks are rare.

The causative agent of the disease is the fungus *Coccidioides immitis* and present knowledge indicates that the infection is usually acquired by inhaling dust contaminated by the spores. Infection through an open skin wound may occur but is uncommon. The disease is not transmitted from person to person and affects females more frequently than males, in the ratio of 2 to 1. Coccidioidal granuloma, on the other hand, is more prevalent in males, in the ratio 4 to 1 (2, 3).

The early manifestations of acute coccidioidomycosis have been completely described by Faber, Smith, and Dickson (5), Dickson (3), Gifford (4), and Farness (6). The symptoms closely parallel those of influenza or bronchopneumonia. The onset is sudden, with headache, weakness, anorexia, nausea and occasional vomiting, dry hacking cough, pleuritic pain, occasionally chills, night sweats, fever and malaise.

Faber, Smith, and Dickson (5) define two stages in the acute infection. They state that owing to the character of the symptoms, the first stage is usually undiagnosed but that it is followed by a *spectacular* second stage, characterized by the appearance of erythema nodosum, arthritis, and conjunctivitis. This appears to be particularly true of San Joaquin Valley cases. (Typical erythema nodosum did not appear in the cases to be reported here.)

The diagnosis is made by the finding of the typical double-contoured spherules in the sputum, a positive coccidioidin reaction (in the group to be considered the first positive reactions were obtained at twenty-six days), positive agglutination tests, animal inoculation, leukocytosis, and eosinophilia.

In only one of a combined series of 700 acute cases (in California) did the fatal granulomatous form develop (5), in this case meningitis. Prompt recovery is the rule, although the patient may suffer from weakness and loss of weight for several months. The relation of the acute to the chronic form is unknown, but Dickson (2, 3) believes that the latter is due to generalized dissemination through the blood stream.

This report will deal specifically with a group of college students who presumably contracted the disease at the same time and place. During a three-day trip to an endemic area, 7 of the 14 students were subjected to particularly dusty conditions

and all 7 contracted the disease. All eventually became positive to coccidioidin tests and all showed positive x-ray findings in varying degrees.

ROENTGEN FINDINGS

We have found no reference to the primary form of coccidioidomycosis in the roentgen literature, though roentgen findings have been described in the general literature by Faber, Smith, and Dickson (5). We quote: "Fuzzy densities were seen at the lung roots extending for variable distances into the lung fields, in some instances out to the periphery and having the appearance of consolidation with lobar distribution. The picture was that of bronchopneumonia indistinguishable from that seen in so-called 'epituberculosis.' In one instance a small interlobar effusion was found. In the course of a few weeks the pulmonary densities cleared remarkably." These writers state further: "As yet we have seen no x-ray studies of the chest during the first stage. The pleural pain common at that time suggests that peripheral lesions might already be present."

Farness (6) gives a similar description, stating that "x-rays show hilar thickening and dense shadows scattered through the pulmonary fields." His description covers both acute and chronic cases and, judging from the biographical data, it is probable that only one or two acute cases were included. The reports indicate a more severe and fatal form than that seen in our group. One case of a miliary type was included, but one cannot judge whether this was acute, subacute, or chronic. Carter (7) states that miliary dissemination is probably the rule. (Carter's report deals with the chronic form.)

The most complete report on the roentgen findings in coccidioidal granuloma is that of Carter (7), dealing with the chronic or granulomatous form. His findings were similar to those already mentioned, with additional emphasis on the frequency of cavitation and pleurisy.

This report will deal with the x-ray appearance of first-stage and second-stage lesions as seen in our group of seven cases. As it may affect the pathological picture, it should be stated that these patients were non-residents of any endemic area and presumably had no immunity to the disease. Full blown "Valley fever" is uncommon among older residents of endemic areas (8).

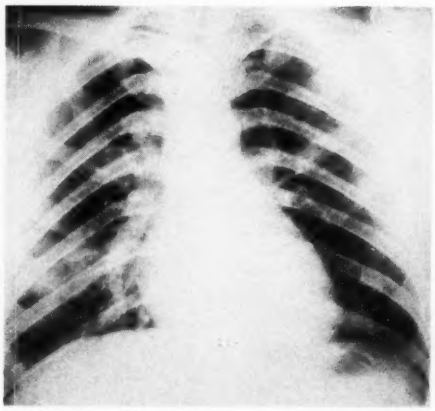
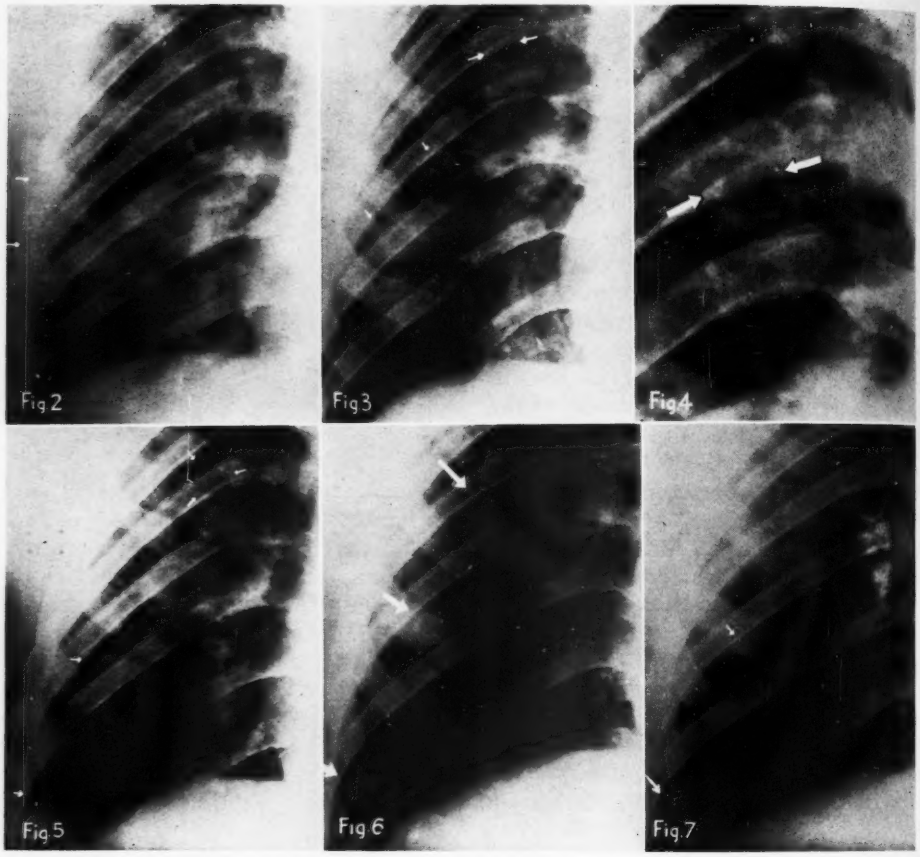


Fig. 1. Case 1: Roentgenogram made on third day of illness, showing multiple parenchymal opaque areas simulating a metastatic process.

In 2 of the 7 patients, roentgenograms were made on the third day from the onset of symptoms; in 4 between the seventh and fourteenth day; in 1 on the twenty-first day. All 7 cases gave positive x-ray findings, but these varied considerably as to the extent of the involvement.

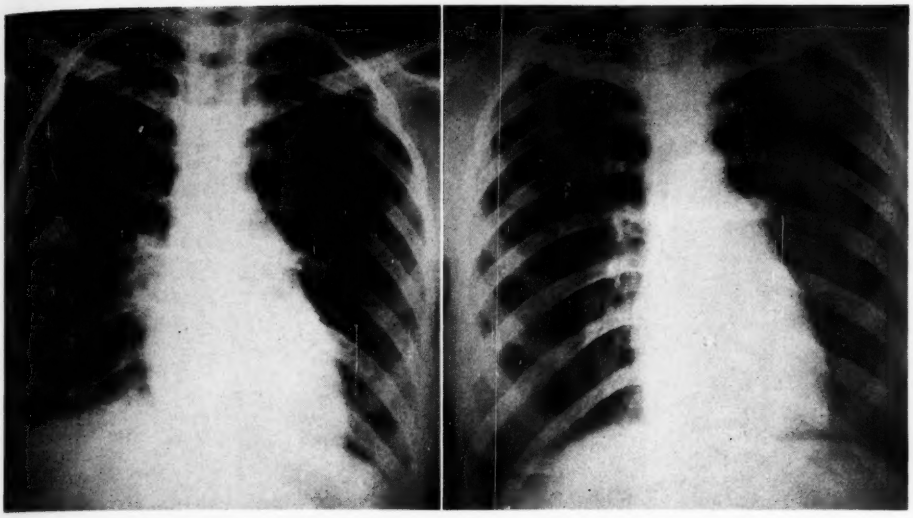
Our cases suggest two types of primary reaction: one a more severe infection with multiple lesions from the start (Fig. 1); the second a milder type with solitary or few lesions, running a more benign and shorter course (Fig. 8). The severe type with multiple lesions may be progressive, with new lesions appearing over several weeks, some going on to cavity formation (Fig. 3). Cavities seem to form and close fairly rapidly. Many of the lesions show central transparency at about three to four weeks, suggesting necrosis or caseation (Fig. 5). Our one case of this type has one small cavity remaining after one year (Fig. 7). Another cavity closed after a few weeks. Several other lesions have re-



Figs. 2–7. Case 1: Fig. 2, taken on the fourth day of illness, shows nodular lesions at the right base. On the twenty-first day of illness (Fig. 3) a cavity was demonstrable under the costochondral junction, right second rib, and there was some contraction of the other lesions. A detail of the cavity is shown in Fig. 4. By the twenty-ninth day (Fig. 5) the cavity was closing and there was central softening in several lesions. Note absence of any marked hilar reaction. Fig. 6, seventy-second day of illness (10th week), shows the lesions contracting, with central transparency. At the end of a year (Fig. 7) a single nodule and one cyst-like shadow remain, though the patient is clinically well.

mained as homogeneous nodules, simulating Assmann's foci of tuberculosis (Case 1, Figs. 1–7).

The majority of cases show solitary or a few fairly sharply contoured spherical, opaque areas having a peripheral distribution (Fig. 8). The location is usually opposite or posterior to the hilum, in the apex of the lower lobe, or the lower part of the upper lobe. Apices appear to be spared but lesions may be present at the bases, and pleural "tenting" at the base was present in one case. The lesions are usually homogeneous in density and many of them appear distinctly nodular. In the majority of the cases some shrinking is noticeable in about one week. Some lesions remain as solitary homogeneous nodules about one-fourth the size of the original focus (Fig. 9). Others are absorbed, leaving an inconspicuous parenchymal scar. No calcification can be demonstrated in any of these nodules as yet (one year). Increase in hilar density has not been a prominent feature in any of our cases. Lateral examination usually shows the opacities to be peripheral and posterior to the hilum.



Figs. 8 and 9. Case 2: Fig. 8 (left), second day of illness, shows consolidated areas opposite and posterior to the right hilum. A lateral projection showed no hilar increase. Fig. 9, one year from onset, shows a residual nodule (presumably fibrocaseous); patient clinically well.

DIFFERENTIAL DIAGNOSIS

It is doubtful if acute coccidioidomycosis can be diagnosed by x-rays alone, but the roentgenograms may be suggestive enough to point the way to a correct diagnosis. The multiple lesion type may simulate metastatic disease or scattered embolic foci of infection (beginning abscesses), but the clinical picture, eosinophilia, finding of spherules in the sputum, and (later) agglutination reaction and the coccidioidin test will settle the diagnosis.

The milder cases (those with solitary or few lesions) may simulate pneumonia, but bronchopneumonia usually shows more "patchy density" and less homogeneity. Areas of opacity in lobar and pseudolobar pneumonias are usually larger and not so spherical. An "epituberculosis" reaction is often the first diagnosis, but primary coccidioides lesions fail to show the fading off into the surrounding lung fields, are more spherical, lack the marked hilar reaction, and usually clear more rapidly. Symptoms are more severe in coccidioides. Some lesions may simulate a cyst or tumor but the history, clinical picture, and laboratory findings should make differentiation possible.

Solitary lesions may simulate pneumonic infiltrations, but all appear to have little in common with the "raisin-on-the-stem" appearance of basal bronchopneumonia. They usually are and remain more circumscribed than an early pneumonic patch. Lesions posterior to the hilum are more likely to be confused with a beginning pneumonia or with the early stages of lung abscess.

Friedländer's bacillus pneumonia may be simulated by severe cases with multiple foci.

We have no information as to the roentgen appearance in other *primary* fungus infections. The subject of the roentgenologic aspects of bronchomycosis has been thoroughly presented by Doub (9), whose cases included blastomycosis, actinomycosis, moniliasis, aspergillosis, coccidioidal granuloma, and streptothricosis. Most of these cases were of several months' duration and, with the possible exception of blastomycosis, appear to show little similarity to acute coccidioidomycosis. This does not apply to the granulomatous form, however, as the evidence indicates that its appearance may often be quite similar to that of several of the bronchomycoses.

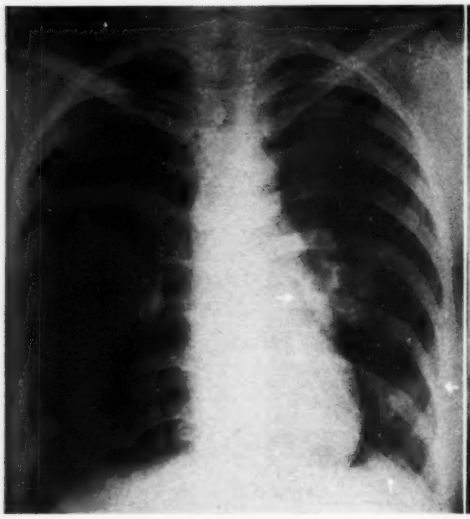


Fig. 10. Case 4: Roentgenogram taken on thirteenth day of illness. Consolidated areas posterior to right hilum and at left base. Some diaphragmatic "tenting" on left.

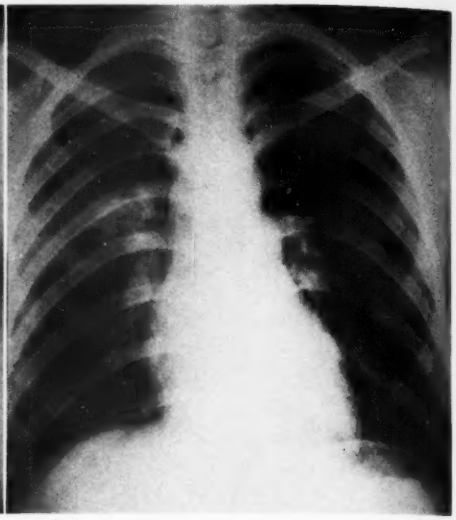


Fig. 11. Case 6: Roentgenogram taken on fourteenth day of illness. Lesion on right is parenchymal. Lateral projection showed it posterior to hilum.

CASE REPORTS

CASE 1: O. C., age 21, male student, had sudden onset of fever and weakness nine days after exposure, and was hospitalized three days later, when cough, nervousness, anorexia, and continued fever to 103° demanded medical attention. His history included two summers' residence in the San Joaquin Valley. The course was severe, with fever, night sweats, and productive cough, gradually subsiding in six weeks, with clinical recovery in three or four months. There was no erythema nodosum. The white cell count was 17,700, with 8 per cent eosinophils. Spherules were found in the sputum. The coccidioidin test was positive (26th day). Initial x-ray examination on the third day showed multiple areas of peripheral density (Fig. 1). Three weeks later cavities appeared (Figs. 3 and 4), one to close with regression of many pulmonary lesions, and one to remain with other residual signs one year later (Figs. 6 and 7).

CASE 2: A. S., age 19, female student, had severe backache ten days after exposure, this initial symptom being followed shortly by fever, night sweats, anorexia, and headache, with persistent non-productive cough appearing two days later. Past history showed only slight exposure to the San Joaquin Valley. The patient was hospitalized for two weeks (12 lb. weight loss); headache, weakness, and cough remained five to six weeks, and she did not feel entirely well for four or five months. There was no erythema nodosum. The white cell count was 11,600, with 5 per cent eosinophils. Spherules were recovered from the sputum. The coccidioidin test was positive (27th day). The initial chest film, on the third day, showed pulmonary involvement (Fig. 8). Most of the areas cleared promptly with the clinical improvement, but some change remains at one year (Fig. 9).

CASE 3: W. G., age 24, male student, had symptoms nearly two weeks after exposure, initiated by hacking cough, anorexia, feeling of oppression in the chest, fever, and frontal headache. His history indicated but minimal association with any known endemic area. The course was relatively mild, without hospitalization. Fever and night sweats lasted about a week; cough four weeks; anorexia six weeks, with some weight loss. The white cell count was 15,000, with 5 per cent eosinophils. There were no sputum findings. The coccidioidin test was positive (30th day). Roentgen changes were slight, consisting only in an opaque area posterior to the hilum.

CASE 4: B. M., age 20, female student, experienced symptoms two weeks after exposure, consisting in sudden chills, fever, anorexia, malaise, and severe frontal headache, with diarrhea and vomiting on the second day. She had had but slight contact with the San Joaquin Valley. Fever of 102°, with additional symptoms of cough and backache, initiated a five-day period of hospitalization. The major symptoms soon decreased, but cough continued one month and anorexia six weeks after onset. Some skin lesions unlike erythema nodosum developed during the hospital stay. The white cell count was 15,800, with 6 per cent eosinophils. There were no sputum findings. The coccidioidin

test was positive (30th day). A chest film on the thirteenth day of illness showed definite changes (Fig. 10), which had completely disappeared by the forty-second day.

CASE 5: R. R., age 19, female student, had never been in the San Joaquin Valley. About nine days after exposure she had fever, night sweats, generalized aching, and anorexia continuing for three weeks. There were initial nausea and vomiting, and also very severe backache and pleural pain, with persistent non-productive cough present from the fifth day. The patient was not hospitalized. Cough and headache were present for one month, and loss of weight and strength lasted several months. The white cell count was 11,700, with 10 per cent eosinophils. Spherules were found in the sputum. The coccidioidin test was positive (30th day). Chest films showed unquestioned evidence of peripheral involvement in the infraclavicular area and at the costophrenic angle.

CASE 6: D. S., age 20, female student, had abrupt onset two weeks after exposure, with pain in chest and neck, cough, fever, anorexia, and generalized aching. This patient had lived nine years during childhood in Sacramento, and had crossed the San Joaquin Valley numerous times. The course was relatively mild, with most of the symptoms gone in three weeks; no hospitalization. Headache and fatigability remained several months. No erythema nodosum developed. The white cell count was 11,000, with 8 per cent eosinophils. Spherules were found in the sputum. The coccidioidin test was positive (38th day). Chest films taken on the fourteenth day of illness show definite changes (Fig. 11), which disappeared by the fifth week.

CASE 7: J. B., age 21, female student, with history of occasional trips across the San Joaquin Valley, developed cough and headache three weeks after exposure, while on a hayride. She had no other symptoms. X-ray examination showed patchy density at the right base and at the costophrenic angle. The white cell count was 12,000, with 6 per cent eosinophils. Recovery was uneventful.

SUMMARY

Acute coccidioidomycotic lesions (as found in this group) are usually solitary or few in number but may occasionally be multiple. Early lesions are usually spherical and peripheral and a marked hilar reaction is not a prominent feature. Lesions may simulate solitary or multiple metastatic nodules but are most commonly confused with primary tuberculosis or pneumonia.

Note: We express our grateful appreciation to Drs. Burt L. Davis, Ruth T. Smith, C. E. Smith, and Arthur Bloomfield for clinical material and to Dr. Robert Newell for certain of the roentgenograms used in this paper.

261 Hamilton Ave., Palo Alto, Calif.

REFERENCES

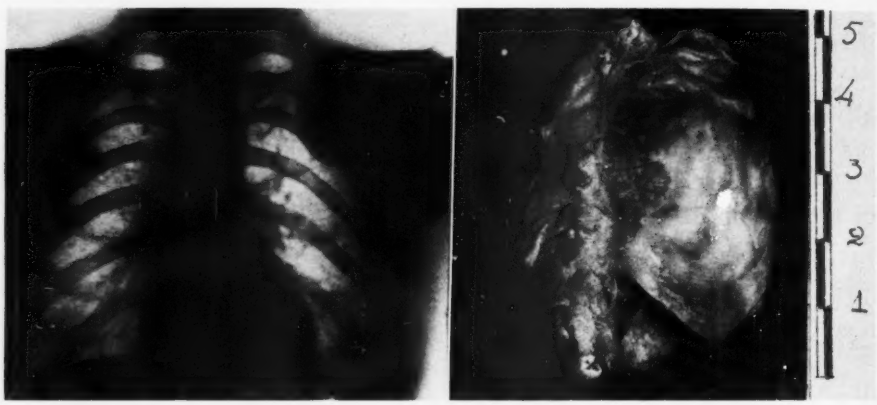
1. WERNICKE, R.: Ueber einen Protozoenbefund bei Mycosis fungoides. Centralbl. f. Bakt. **12:** 859, 1892.
2. DICKSON, E. C.: Coccidioides Infection. Arch. Int. Med. **59:** 1029–1044, June 1937.
3. DICKSON, E. C.: Coccidioidomycosis. J. A. M. A. **111:** 1362–1364, Oct. 8, 1938.
4. DICKSON, E. C., AND GIFFORD, MYRNIE A.: Coccidioides Infection (Coccidioidomycosis). Arch. Int. Med. **62:** 853–871, November 1938.
5. FABER, H. K., SMITH, C. E., AND DICKSON, E. C.: Acute Coccidioidomycosis with Erythema Nodosum in Children. J. Pediat. **15:** 163–171, August 1939.
6. FARNESS, O. J.: Coccidioidomycosis. J. A. M. A. **116:** 1749–1752, April 19, 1941.
7. CARTER, RAY A.: Coccidioidal Granuloma: Roentgen Diagnosis. Am. J. Roentgenol. **25:** 715–738, June 1931.
8. THORNER, JULIET E.: Coccidioidomycosis. California & Western Med. **54:** 12–15, January 1941.
9. DOUB, HOWARD P.: Roentgenologic Aspects of Bronchomycosis. Radiology **34:** 267–275, March 1940.

The Roentgen Diagnosis of Neurinoma of the Thorax[1]

DR. I. N. ODESSKY

Moscow, U.S.S.R.

NEURINOMAS of the thoracic wall are of rare occurrence, as has been pointed out by Lenk and by Kienböck and Rösler (1932). We were able in the literature available to us to find but a single case resembling the one recorded here, namely, that reported by Canigiani (1931). He describes a roentgen shadow similar in shape and form to that in our patient, but situated somewhat lower in the chest. It was at first attributed to an encapsulated pleurisy; later to an echinococcus cyst or neurofibroma. The latter diagnosis was considered more probable because of the presence of a cutaneous neurofibromatosis with multiple pigmented spots, and proved at operation to be correct.



Figs. 1 and 2. Case 1: Roentgenogram showing the oval shadow in the left lung, and the tumor, which proved to be a neurinoma.

CASE 1: A thirty-seven-year-old woman was admitted to the hospital with a diagnosis of echinococcus cyst of the lung. Her chief complaints were general weakness, pain beneath the left scapula, high evening temperature, and night sweats. Physical examination revealed nothing of significance. The blood count was as follows: red cells 3,920,000; hemoglobin 68 per cent; color index 0.87; white cells 8,000 (8 per cent eosinophils, 2 per cent stab forms, 59.5 per cent neutrophils, 26 per cent lymphocytes, 4.5 per cent monocytes).

Roentgen examination, April 11, 1937, showed an oval homogeneous shadow in the upper part of the left lung, measuring about 7 × 4 cm., close to the chest wall (Fig. 1). It appeared to lie outside the lung, which was otherwise unchanged. There was no interference with the excursion of the diaphragm.

On the basis of the clinical and roentgen findings an encapsulated exudative pleurisy was suspected, but a tumor could not be excluded. Echinococcus cyst seemed unlikely, as in such cases the shadow is usually spherical and in the middle or lower lobe of the lung.

The patient was operated upon (by Dr. M. A. Egorov and Dr. W. I. Migin) on April 25, 1937. Resection of the second rib revealed a tumor measuring about 5 × 4 cm. (Fig. 2) located extrapleurally and showing areas of caseous degeneration and fragments of nerves at either pole. Histologic examination (Dr. W. A. Klirikov) showed it to be a neurinoma.

A few days after operation the patient's temperature rose, and further roentgen examination showed a shadow (Fig. 3) similar in size, form, and location to that originally seen. Since this disappeared under subsequent roentgen therapy, it was concluded that it was a hematoma rather than a second neurinoma, as the latter tumor is known to be radioresistant.

[1] From the Department of Roentgenology, Ostroumov Hospital and 3d Moscow State Medical Institute (Director A. Zeitlin, M.D., Professor of Roentgenology). Accepted for publication in March 1938.

In the interests of differential diagnosis two roentgenograms are reproduced here showing shadows similar to that in the case recorded, but with a different anatomical substrate. Figure 4 shows a shadow in the middle of the left lung diagnosed, on the basis of the history, as an encapsulated pleurisy. Figure 5 shows a similar shadow due presumably to a metastatic tumor, as the patient was operated upon for a sarcoma of the cecum.

As stated above, neurinomas of the thoracic wall are unusual, neurinomas of the posterior mediastinum being more common. Kienböck and Rösler in their monograph reviewed the literature from 1870. The total number of cases recorded does not exceed 125, the majority of which were diagnosed only after operation or at autopsy. In only about a quarter of the cases was a diagnosis made on the basis of the roentgenologic and clinical observations.

As described in the literature the thoracic neurinoma appears in the roentgenogram as a homogeneous shadow to one side of the chest, semi-oval or spherical in form with a distinct outline, occupying in most cases the middle of the lung, with its base adjacent to the mid-thoracic spine. It may, however, occupy the upper right or left lobe and sometimes lies near the hilus. The size varies; it may approach that of an infant's head. Anatomically the shadow is seen more frequently in the posterior mediastinum. When the examination is made anteriorly, the shadow is projected in the region of the thoracic vertebrae. This picture is not sufficient, however, for a diagnosis, since a similar shadow is produced by a wide variety of conditions, including pulmonary tumors, teratomas, hydatid and other cysts, aortic aneurysm, and encapsulated pleural exudates. Clinical methods also, with rare exceptions, fail to produce confirmatory data. Neurinomas are not infrequently discovered incidentally in the course of a routine roentgen examination.

If a diagnosis is to be made, the first step consists in excluding those lesions producing a similar roentgen picture in the dorso-ventral position but situated in the anterior mediastinum (Bobretzkaja and Heinismann, 1935). Encapsulated exudates present in the posterior mediastinum, as well as malignant tumors, can usually be ruled out by the history. Echinococcus cysts are of rare occurrence in the posterior mediastinum. The Casoni reaction is useful in such cases but is not infallible. A decisive factor in the favor of a diagnosis of neurinoma is the constancy of the roentgen picture. Also of

Fig. 3. Case 1: Postoperative roentgenogram, showing a shadow which disappeared following radiotherapy, and thus proved to be a hematoma rather than a second neurinoma.

significance is the good general condition of the patient. Neurofibromatous lesions in the skin and elsewhere are confirmatory evidence of the character of the tumor.

Two cases are of interest in this connection.

CASE 2: A man of thirty-one was referred for x-ray examination of the chest because of an attack of grippe. An area of density was seen in the lower part of the right lung, serving as the background for an oval shadow near the thoracic vertebrae.

Before his present illness the patient had experienced some awkwardness and a disagreeable sensation referable to the right side of the back. He had also suffered from hoarseness and a cough, recurring periodically. He was able to continue at his work, however, ate well, and even gained weight. In the winter of 1925 he suffered an attack of grippe and the following summer he complained of cough with purulent sputum and pain in the chest, which, however, soon disappeared.

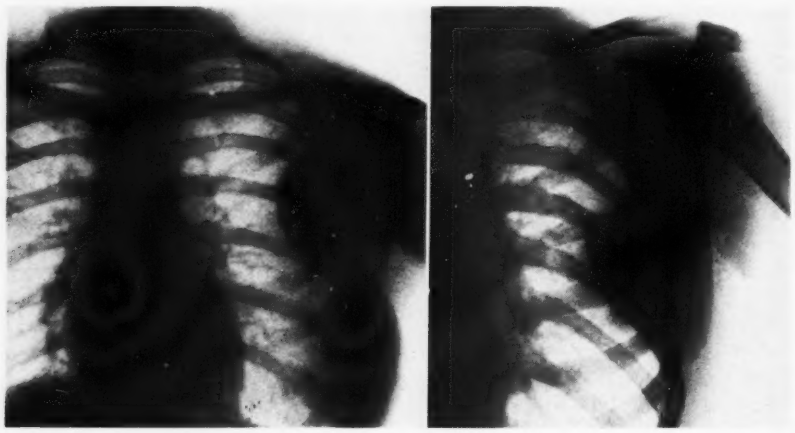
There was some dullness to percussion on the right side, and the heart sounds were weak; expansion of the chest on inhalation was limited on that side. Physical examination and clinical laboratory tests showed nothing of significance.

Roentgen examination showed in the middle of the right lung a round homogeneous shadow, the size of a child's head, with distinct boundaries. It appeared to blend with the heart shadow but in the oblique position was seen to be distinct from the latter. In the frontal position it appeared to lie in the posterior mediastinum. A posterior view (Fig. 6) showed it even more clearly.

This patient was under observation for four years, during which repeated roentgen examinations failed to show any change in the size or appearance of the lesion. The Wassermann reaction and the Casoni and Weinberg tests for hydatid disease were repeatedly negative. The probable diagnosis, based upon the location, form, homogeneous character, and definite contour of the shadow, is neurinoma. A cystic tumor, however, cannot be excluded, though this would more probably be located in the anterior mediastinum. A malignant growth is ruled out by the roentgen findings.

CASE 3: A woman, thirty-one years old, complained of pain in the back and weakness of the extremities. She experienced a sense of numbness in the lower abdomen and legs and could not walk unaided. A year and a half before admission she had undergone an operation for a uterine myoma.

Roentgen study of the thoracic spine revealed a distinctly outlined shadow in this region, and some destruction of the head and neck of the seventh rib. Chest films showed a round, clearly outlined shadow in the middle of the right lung, 6 or 7 cm. in diameter, adjacent to the thoracic spine (Fig. 7). Examination in the lateral position indicated a location in the posterior mediastinum. A diagnosis of tumor was made and the patient was discharged. Two years later she was again examined, at which time no further changes had occurred, thus excluding a malignant growth. The subsequent history is recorded by Bobretzkaja and Heinismann (1935).



Figs. 4 and 5. Shadows similar to that produced by the neurinoma in Case 1. That in the roentgenogram on the left is attributed, on the basis of the history, to an encapsulated pleurisy. That on the right is due presumably to a metastatic tumor.

The patient was operated upon because of exacerbation of symptoms, and the tumor was found histologically to be a neurinoma and sarcoma.

The two cases just recorded (Case 2 and Case 3) belong in the group with round paramediastinal shadows. The roentgen pictures were similar. In Case 2 the constancy of the picture over a period of several years, together with the possibility of the existence of the tumor long before its discovery and the good general condition of the patient, led us to a diagnosis of neurinoma after the exclusion of other lesions producing a similar picture.

In Case 3 beside the tumor a destructive process in the rib was found. Clinical data and long observation indicated the

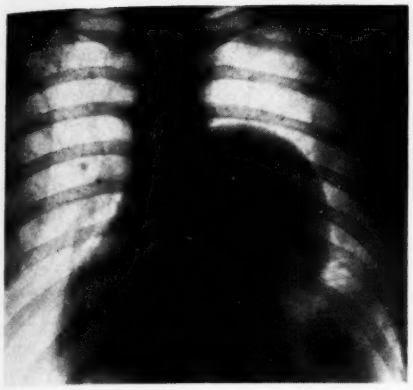


Fig. 6. Case 2: Thoracic neurinoma, posterior roentgenogram.

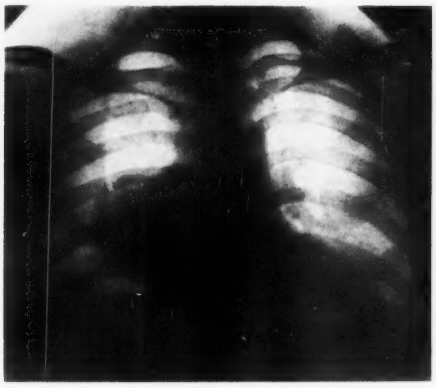


Fig. 7. Case 3: Posterior mediastinal tumor, diagnosed as a neurinoma.

benign nature of the process. Later surgical intervention following an exacerbation of symptoms permitted histologic study of the tumor, revealing in one specimen neurofibroma, in another sarcoma. The change in the patient's condition must be ascribed to malignant change in the tumor.

CONCLUSIONS

The roentgen picture of neurinoma of the thorax has been described on the basis of personal observations and the literature. The diagnosis of neurinoma presents some difficulties, and the incidence is probably much greater than is supposed, as the lesion is not always recognized during the life of the patient. There are no pathognomonic symptoms.

Harrington (1934) states that of 41 intrathoracic tumors removed by transpleural operation, 8 were found to be neurofibromas. In all cases where there is prolonged illness and an unchanging roentgen picture the possibility of a neurinoma should be considered. The final diagnosis, however, can be established only by histologic examination.

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REFERENCES

BOBRETZKAJA, W. N., AND HEINISMANN, J. I.: Beiträge zur Röntgendiagnostik der mediastinalen Neurinome. Fortschr. a. d. Geb. d. Röntgenstrahlen **52:** 191–199, August 1935.

CANIGIANI, T.: Ueber die intrathorakalen Neurofibrome und ihre Differentialdiagnose. Röntgenpraxis **3:** 214–219, March 1, 1931.

HARRINGTON, S. W.: Right Intrathoracic Neurofibroma. Surg. Clin. North America **14:** 628–631, June 1934.

KIENBÖCK, R., AND RÖSLER, H.: Neurofibromatose. Archiv und Atlas der normalen und pathologischen Anatomie in typischen Röntgenbildern. Fortschr. a. d. Geb. d. Röntgenstrahlen, Supp. 42, 1932.

Carcinoma of the Male Breast[1]

MAURICE D. SACHS, M.D.

University of Oregon Medical School, Portland, Oregon

"It was my original design to follow up that work with a description of the malignant diseases, but upon approaching the subject I found that much confusion had been created by the authors."

—Sir Astley Cooper, 1845

Since Cooper's time (13), rapid progress has been made in the diagnostic and therapeutic knowledge of carcinoma with resultant curtailment of the disease. Ability to recognize and satisfactorily treat carcinoma of the breast, however, particularly in the male, has lagged considerably. The paucity of information regarding male breast carcinomas is a direct result of the rarity of this condition. In general, it is agreed that carcinoma of the breast manifests itself alike in the male and female (1, 4, 6, 7, 19, 49), although a few articles on the subject have cast some doubt on the correctness of this belief (12, 22, 25, 26, 39, 41, 50, 51).

In an effort to bring more light on the subject of carcinoma of the male breast, a questionnaire pertaining to symptomatology, clinical aspects, therapy, and end-results was submitted to leading radiologists, surgeons, and pathologists practising in the United States and Canada. The co-operation of a relatively large group of these has made available for analysis 205 cases, with pathological data in 178. Three patients refused either biopsy or surgery, and in 24 cases no pathological studies were made. The clinical and radiographic evidence was sufficiently positive, however, to warrant a diagnosis of malignant growth

In addition to the above series, 172 cases appearing in the literature were analyzed, excluding 47 reported by Gilbert (19) and 154 by Wainwright (61), plus 264 abstracted by the latter writer. Undoubtedly some of the present series of 172 will duplicate cases collected by Wainwright.

HISTORICAL

Franciscus Arcaeus (1494–1573) and Ambroïse Paré (Paris, 1510–1590) were among the first to report on carcinoma of the breast. In the following century Thomas Bartholin (Copenhagen, 1616–1680) wrote on cancer of the breast. Gilbert (19) in a recent article quoted Wolff to the effect that the case mentioned by Bartholin was probably in a female rather than a male. Thomas Heister (1700–1750) wrote an excellent monograph on the subject. One of the first comprehensive studies was written by Poirier (Paris Thèse, 1883). He was soon followed by Schuchardt (52, 53, 54) in 1885, 1887, and 1891, and Williams (64) in 1889.

In the twentieth century this interesting subject was studied by many investigators, including Warfield (63), Judd and Sistrunk (26), Judd and Morse (25), Wainwright (61), and Gilbert (19). The foregoing authors attempted a systematic study of male breast carcinomas; occasional single cases were also reported in the literature (5, 6, 7, 8, 9, 10, 36, 42, 53).

STATISTICAL STUDY

Incidence: In the present series the ratio of male breast carcinomas to all male carcinomas is 0.38 per cent and to female breast cancers 1.32 per cent. The United States census report of 1900 stated that the incidence of breast carcinoma in the male was 0.7 per cent whereas in the female it was 15.7 per cent. The ratio of male breast carcinomas to all male carcinomas (as shown in Table I) ranges from 0.38 to 1.5 per cent. The mean average is 0.7 per cent. The ratio to female breast cancers varies from 0.08 to 3.0 per cent, with a mean average of 1.16 per cent.

[1] Read before the Radiological Society of North America, at the Twenty-sixth Annual Meeting, Cleveland, Ohio, Dec. 2–6, 1940.

TABLE I: INCIDENCE OF CARCINOMA OF THE BREAST IN THE MALE

Authors	In relation to all other male cancer	In relation to female breast cancer
Author's series (1940)	0.38%	1.32%
Williams (1889)	1.0	0.7
Pack and LeFevre (Gilbert, 1933)	0.41	1.25
Pondville Hospital (1940)	0.25	..
U. S. Census Report 1900 (Moore)	0.7	..
Schreiner (1932)	1.25	..
Deaver and MacFarland (1917)	1.5	..
England and Wales Census 1926 (Gilbert)	..	0.08
Schuchardt (1884)	..	2.0
Judd and Morse (1926)	..	0.9
Judd and Sistrunk (1914)	..	3.0
Rosh (1931)	..	2.0
Keyser (1904)	..	0.7
Yamamoto (1911)	..	1.08

Age: Reports of the several authors indicate unanimous agreement that cancer of the breast occurs later in life in the male than in the female. Yamamoto (66) found that the average age of the male was 54 years (167 cases) as compared to 45.3 years in the opposite sex (11,654 cases). Keyser (27) stated that in his series the average age in the male was 61 as compared to 49.2 years in the female. Wainwright (61) reported an average of 52.6 years in the male and 45–49 in the female. Bryan (10) cited a case of carcinoma of the breast in a boy of twelve, Blodgett (8) in a youth of fourteen years and eight months. The oldest patient, reported by Lunn (36), was a man 91 years of age.

The author's series revealed an average age in the male of 57.17 years; the youngest patient was 12 and the oldest 86 years.

Race: Carcinoma of the male breast was thought to be predominant in the white race because of reports from institutions in which the majority of patients were woite. It has been reported, however, in almost all nationalities. Ludlow (35) cited a case in a Korean. Wainwright (61) cited a case recorded by Sirrha in a native East Indian and one by Welch in a Kikuyu, of British East Africa. Moustardier (40) described two cases in Madagascar natives. Many examples have been reported in Negroes; Lewis and Rienhoff (34) recorded 3. Of 188 among our 205 cases, 178 were in white patients, 9 in Negroes, and 1 in a Chinese.

TABLE II: AGE INCIDENCE IN CARCINOMA OF THE MALE BREAST IN COMPARISON WITH CARCINOMA OF THE FEMALE BREAST

Age (yrs.)	Author's Series (194 cases) %	Gilbert (47 cases) %	Wainwright* (401 cases) %	Lane-Claypon* (Females) (8,053 cases) %
10–14	...	...	0.5	1.0
15–19	...	...	0.2	1.0
10–19	**2.1**	...	**0.7**	**2.0**
20–24	...	...	1.5	0.1
25–29	...	...	0.7	1.0
20–29	**1.1**	...	**2.2**	**1.1**
30–34	...	...	1.5	3.9
35–39	...	...	5.7	8.4
30–39	**5.3**	**14.9**	**7.2**	**12.3**
40–44	...	...	8.7	14.7
45–49	...	...	14.0	18.3
40–49	**14.9**	**14.9**	**22.7**	**33.0**
50–54	...	...	13.2	17.2
55–59	...	...	16.2	13.4
50–59	**22.2**	**36.2**	**29.4**	**30.6**
60–64	...	...	17.2	11.2
65–69	...	...	9.2	6.8
60–69	**35.9**	**25.6**	**26.4**	**18.0**
70–74	...	...	8.0	3.4
75–79	...	...	2.0	1.2
70–79	**15.8**	**6.3**	**10.0**	**4.6**
80–84	...	...	0.75	0.2
85–89	...	...	0.25	0.2
80–89	**2.7**	**2.1**	**1.0**	**0.4**
90–94	...	...	2.5	...
	100.0	100.0	102.1	102.0

* The Wainwright and Lane-Claypon series were divided into five-year groups, but for simplification the author has taken the liberty of compiling their series into ten-year groups as well as five-year groups.

SYMPTOMATOLOGY

Duration of Symptoms: Wainwright (61) reported an average duration of symptoms of 2.4, Poirier (1883) 2.5, Judd and Morse (25) 2.75, Williams (64) 3.16, and Memorial Hospital (19) 3.33 years. The average duration of symptoms before our patients consulted a physician was 1.14 years. Sixty-one per cent of these patients consulted a doctor within one year after the lesion was noticed and 87.42 per cent within two years. Wainwright (61) stated that 46.6 per cent visited a physician in the first year and 55 per cent within the first two years. In 1928, Lane-Claypon (32) reported 79 per cent and over 90 per cent of women with breast carcinoma as visiting a

TABLE III: DURATION OF SYMPTOMS IN CARCINOMA OF THE MALE AND FEMALE BREAST

	Author's Series (174 cases) %	Wainwright (342 cases) %	Lane-Claypon (Females) (1,493 cases) %
0–6 mos.	38.5	23.3	56.93
7–12 mos.	22.5	23.3	22.3
13–23 mos.	26.4	7.9	11.5
2–3 yrs.	5.8	25.8	8.8
4–5 yrs	1.7	8.5	..
6–9 yrs.	1.7	4.4	..
10–14 yrs.	2.3	3.0	..
15–19 yrs.	1.1	1.4	..
20–34 yrs.	..	1.4	..

doctor within one and two years, respectively. (See Table III.)

Several of our series presented a long history of tumor with sudden rapid growth. These must have been benign tumors which had undergone malignant change. Judd and Morse (25) cited a case with an eighteen-year history and sudden increase in size within the last two years. Eisendradth and Owens (25) reported a case with a thirty-five-year history.

Pain: Gilbert (19) reported that pain was present in 27 per cent of cases. Kunath (30) and Andrews and Kampmeier (3) mentioned pain as a frequent and early symptom. In our series, it was present in 38.1 per cent.

Nipple Retraction: Judd and Morse (25) attributed nipple retraction to the small amount of glandular tissue present in the male breast. Gilbert (19) reported nipple retraction in 29 per cent of the cases, Speed (58) in 50 per cent, Williams (64) in 73 per cent. In the author's series it occurred in 33.1 per cent.

Bleeding Nipple: Gilbert (19) found bleeding from the nipple in 8 per cent of the cases, Speed (58) in 50 per cent, Williams (64) in 73 per cent. A review of single cases appearing in the literature shows its presence in 24 per cent. A bleeding nipple was present in 14.6 per cent of our cases.

Ulceration: Cheatle and Cutler (11) stated that ulceration is a common finding; Gilbert (19) recorded the presence of ulceration in 29 per cent of cases; Andrews and Kampmeier (3) found it in 30 per cent of cases and noted its early occurrence; in the abstracted literature its incidence is 33 per cent; Wainwright's (61) figure is 38 per cent. Ulceration does not seem to depend on the duration of the tumor or its size; it generally occurs within the first two years. It was observed in 25.5 per cent of our cases.

TRAUMA

The relationship of trauma to tumors in this era of compensation insurance presents a problem deserving much consideration. There are several controversial opinions as to whether a single injury may be the cause of a tumor. Knox (28) wrote: "It is unscientific to think that a single trauma can produce cancer." Murphy (42) stated that cancer in the breast very frequently is the result of a mild single trauma. The consensus is that cancer may be caused by chronic occupational trauma.

It is appropriate at this time to recall Ewing's (16) postulates for tumor caused by trauma: Authenticity and sufficient severity of the trauma must first be established; previous integrity of the wounded part must be shown; identity of the injured area with the site of the neoplastic growth must be demonstrated; the tumor must be shown to be of a type which could result from trauma; and a proper interval of time must be proved to have elapsed. Experimentally, Ribbert (28) was unable to produce any tumors in animals as the result of trauma. Balforth (28) traumatized sea urchin eggs in the gastrula stage by displacement, and found no tumors; the most he could produce were cysts. Knox (29) was able to show in mice that constant massage over a definite area repeated for a few days would liberate metastatic emboli.

Gilbert (19) reported a history of trauma in 29 per cent of his cases (14 cases—12 single injuries, and 2 occupational). Billroth (61) described a carcinoma that had developed six months after a nipple gunshot wound, and Bryan (10) recorded a case in a lad of twelve developing within a short time after he was struck in the breast by a golf ball. Breast carcinomas have been observed in shoemakers, carpenters,

TABLE IV: SIDE INVOLVED IN CARCINOMA OF THE BREAST IN MALES AND FEMALES

Author	No. of cases	Right breast	Left breast	Bilateral involvement
Author's series (1940)	205	99	106	3
Cumston (1920)	266	139	126	1
Fitzwilliams (1924)	296	148	143	5
Wainwright (1927)	336	163	170	3
Gilbert (1933)	47	20	26	1
Lane-Claypon (females) (1924)	13,909	6,907	7,002	...
Lane-Claypon (females) (1928)	1,767	809	958	...

and postmen. Lunn (36) reported a case of cancer in a man 91 years of age as a result of friction from braces, and Bell (6) a case in a carpenter due to constant pressure of the maul. Of our collected cases 29.3 per cent gave a history of previous trauma. Eight patients stated that trauma was acute and tumor appeared from one to seven months after the injury, 2 of these being young boys twelve years of age who were hit by baseballs. One other patient, with a gunshot wound through the right nipple, developed a tumor, in the scar, four years later.

SIDE INVOLVED

Statistics in the literature reveal that carcinoma occurs almost equally in the two breasts. The left breast, in most instances, was found to be involved more frequently than the right. In our series of 205 cases the right breast was involved 99 times and the left 106. Bilateral involvement was present in 3 cases. These figures compare favorably with those of Fitzwilliams (17), Wainwright (61), Cumston (14), and Gilbert (19), and with Lane-Claypon's (32) for females.

CLINICAL CLASSIFICATION

Primary Operable: A review of 75 cases in the literature showed 58 per cent to be operable. Gilbert (19) reported that 58 per cent of his cases were operable, and Bailey (5) 66 per cent. At the time of examination 73.8 per cent of our cases were considered by the surgeons to be operable and 18.55 per cent were regarded as inoperable; in 7.65 per cent no mention was made as to operability.

TABLE V: PATHOLOGY IN CARCINOMA OF THE MALE BREAST

	Author's Series (178 cases) %	Wainwright (78 cases) %	Gilbert (47 cases) %
Adenocarcinoma	40.70*	17.0†	19.15
Scirrhous	19.09	49.0	4.25
Medullary	9.55	18.0	...
Simplex	8.98	3.7	53.19
Carcinoma	15.73	...	...
Gelatinous	0.56	3.7	...
Squamous-cell or basal-cell	0.56	9.0	2.13
Paget's	1.12	...	...
Carcinoma (aspiration)	0.56	...	10.64
Sarcoma	2.24	...	...
Premalignant adenofibroma	1.12	...	...
No record	...	...	10.64

* Includes one intraductal papilloma.
† Includes three intraductal papillomas, one comedo type.

Axillary Nodes at Time of Examination: Axillary nodes were present in 25 per cent of Gilbert's (19) series. Speed (58) gives their incidence as 60 per cent; Joll (24) 60 per cent; Williams (64) 63 per cent; Wainwright (61) 68 per cent. Williams (64) stated that axillary metastases are present in 73 per cent of cancers of the female breast. In 48.3 per cent of our cases axillary nodes were present at the initial examination.

Pathology: Male breast carcinomas are classified histologically in the same groups as carcinoma of the female breast, namely, adenocarcinoma, scirrhous carcinoma, medullary carcinoma, and carcinoma simplex. Sarcoma, squamous-cell, and basal-cell carcinomas are rare. Wainwright (61) remarked that in his histological studies he was unable to distinguish between male and female breast carcinomas.

Pathological details were available in 178 of our cases. The predominant histology was adenocarcinoma, 40.7 per cent; scirrhous carcinoma was present in 19.09 per cent, medullary in 9.55 per cent, simplex in 8.98 per cent, sarcoma in 2.24 per cent, squamous-cell carcinoma in 0.56 per cent, and Paget's disease of the nipple in 1.12 per

cent. In Table V our pathological findings are compared with those of Gilbert (19) and Wainwright (61).

METASTASIS

Recurrences: Gilbert (19) reported that 40.4 per cent of his cases recurred locally. Judd and Morse (25) found the average duration before recurrence to be 19 months, whereas Williams (64) claimed that in the male the average interval was 9.7 months and in the female 26 months. Local recurrences were present in 25.9 per cent of our cases. The majority took place within the first year; 2 patients, however, had recurrences after fifteen years.

Clinical Evidence of Metastasis: Clinically, distant spread was evident in 46.3 per cent of our cases. In most instances the metastases were to the regional lymph nodes (12 cases in the axilla, 2 in the supraclavicular fossa, 2 in the cervical region, 2 in the mediastinum). The brain, spine, and larynx were involved in one case each. Metastases to the lungs were demonstrated by x-ray examination in 27 cases.

Metastasis to Bone: Snow (56) in 1892 described museum specimens of bone, in which the marrow reticulum had been replaced by a tough fibrous tissue which showed the characteristic acini of scirrhous carcinoma. Geschickter and Copeland (18) described bone metastasis histologically as a destruction of the spongiosa and cortex by contact with tumor cells and to a lesser extent by activity of the osteoclasts absorbing spicules of dead bone. According to Geschickter and Copeland extension is *via* the medullary cavity and haversian canals, beginning in the red marrow. The bones react to invasion by converting fibroblasts to osteoblasts, producing an osteoid tissue. Areas of fibro-ostosis with strands of fibrous tissue are transformed into osteoblasts and osteoid tissue bordering on small nests of epithelial cells.

Paget (44) stated that bone marrow hyperemia produces a slowing of the current within the dilated capillaries, thus favoring adherence of tumor cells to the endothelium. Snow (56) thought that cancer cells were in the general circulation and deposited themselves in the bone marrow. This may account for the anemia and cachexia in the late stages of the disease. Von Recklinghausen (60) believed the marrow to be involved first by a hematogenous spread, and the cortex through the nutrient foramen. Geschickter and Copeland (18) explained the frequent involvement of the femoral head as due to the blood vessels in the ligamentum teres. Handley favored a lymphatic permeation, but Neal (43, 45) and others claimed that there are no lymph vessels in bone.

Metastases may be either osteolytic or osteoblastic in type (20, 23, 33, 38, 44, 46, 47, 55, 59). The osteolytic form is characterized by rarefaction and a honeycomb appearance due to a marked lacunar absorption and destruction of the lime salts causing porosis of the osseous tissue. The osteoblastic type is characterized by an irregular increase in bone density, presenting a chalky appearance. There is lacunar absorption, as in the osteolytic form, but the increase in bone density is due to collections of malignant cells plus secondary calcification.

Downs and Hastings (15) noted a definite relationship between the desmoplasia of the primary tumors and the appearance of osteoblastic metastases. They formulated the theory that, "if the primary tumor has the stimulus within itself to cause the growth of young connective tissue, whatever the nature of that stimulus may prove to be, then its cells when they metastasize in bone will exercise the same stimulus, producing osteoplastic bone changes. Conversely, highly cellular tumors without the power of exciting desmoplasia produce osteolytic metastases." Stewart (59) stated that if the primary tumor were medullary then the bone metastases would be destructive and when the primary lesion was scirrhous an osteoplastic bone change would take place. Fowler and many others disagreed with the above statement. Geschickter and Copeland (18) believe that hematogenous metastases produce osteolysis and lymphatic permeation

of cancer cells, resulting in osteoblastic metastases. Leddy (33) does not believe there is any definite relationship between the histology of the primary tumor and the metastasis. Von Recklinghausen (60) was of the opinion that a non-infectious reaction produced an osteoblastic bone involvement. Ginsburg (20) believes that the course is slow in osteoblastic metastases, and that a non-infectious inflammatory reaction may occur with periods of remission. This might account for the periodic relief of pain. To date this problem has not been settled satisfactorily.

Osseous metastases in male breast carcinomas are osteolytic. There have been no reports in the literature of osteoblastic metastases. Gross (20) stated that bone metastasis took place in 20.5 per cent of the cases. Others give the incidence as follows: Williams (64) 26.5 per cent (skull 24 per cent and vertebrae 19.01 per cent); Kaufmann (20) 53.3 per cent; Meyerding, Carman, and Garvin (37) 64 per cent (in 67 out of 1985 cases—64 female and 3 male breast cancers); Ginsburg (20) 74.6 per cent. Geschickter and Copeland (18) state that 5.2 per cent of all male and female breast carcinomas produce bone metastases within five years. Involvement of the skeletal system as demonstrated roentgenologically in 54 cases of the present series is shown in Table VI, together with the findings of Meyerding, Carman, and Garvin (37) and Geschickter and Copeland (18). The chief sites of metastases were: spine 44.4 per cent, pelvis 35.1 per cent, femur and skull 16.6 per cent. The order of bone metastases according to Ewing (16) is sternum, ribs, femur, vertebra, and skull; according to Geschickter and Copeland (18), spine, pelvis, femur, skull, ribs, and humerus. There were 10 pathological fractures in our material for study. According to Ginsburg (20) and Neal (43), pathological fractures are frequent.

Detection of bony metastases is largely dependent upon roentgen examination. Frequently patients will complain of back pain which seems to be localized in bony areas and yet the roentgenograms will appear normal. Lachmann and Whelan (31) and Snure and Maner (57) showed that approximately 20 to 40 per cent of bone decalcification is necessary before visible changes can be demonstrated by x-rays. Meyerding *et al.* (37) showed that the average duration from the time of tumor discovery to the development of metastases is 31.3 months. In cases without surgery bone involvement occurred within 17.09 months.

TABLE VI: BONES INVOLVED BY METASTASIS IN CARCINOMA OF BREAST

	Author's Series (54 cases) %	Meyerding, Carman, and Garvin (67 cases)* %	Geschickter and Copeland (100 cases)* %
Skull	16.66	3.00	13.00
Entire spine	44.44	...	30.00
Cervical spine	...	6.00	...
Dorsal spine	...	16.00	...
Lumbar spine	...	31.00	...
Ribs	31.48	26.00	13.00
Radius	...	...	1.00
Humerus	9.25	...	6.00
Pelvis	44.44	38.00	29.00
Femur	16.66	34.00	22.00
Tibia	...	1.5	1.00
Sternum	3.7	...	4.00
Scapula	1.85	6.00	3.00
Clavicle	...	6.00	3.00
Sacrum	...	6.00	...
Multiple involvement	...	64.00	...
Pathological fracture	12.96	...	...

* Majority carcinomas of female breast.

In recent years, blood phosphatase studies in bone disease by Gutman *et al.* (21), Robison (48), and more recently by Woodard and Higinbotham (65), have opened a new field in the early detection of bone metastasis. One must consider that liver damage and bone dyscrasias of the hyperparathyroid (2), Paget and other types will also produce an increase in blood phosphatase values, and that such diseases must be excluded before such a laboratory procedure can be considered for the early detection of bone metastasis.

It is reasonable to assume, given a carcinoma with clinical complaints localized in a certain area of bony tissue, with increase in phosphatase values, and without positive x-ray findings, that metastases are already present and that palliative radiation therapy should be started. How-

ever, in view of the limited work done to date on phosphatase values some will think it more prudent to wait until further investigations have been made on this subject.

THERAPY

Surgery: In Gilbert's (19) series of 47 cases, simple mastectomies were done in 23.4 per cent, radical mastectomies in 48.9 per cent, axillary dissection in 6.4 per cent, and no surgery in 21.2 per cent. Operation was performed in 64.4 per cent of our cases. Simple mastectomies were done in 22 per cent and radical mastectomies in 42.5 per cent. In 35.6 per cent the lesion was too far advanced for surgery or operation was refused.

Radiation Therapy: Radiation therapy was given to 53.1 per cent of our cases. Of these, 23.8 per cent were given preoperative irradiation, 55.1 per cent postoperative, and 21.1 per cent palliative therapy. A few cases were given low-voltage treatments expressed in terms of erythema doses. Deep therapy (200 kv.) was used in the majority of cases. Fields varied from one large to multiple small fields, with cross-firing of the lesion. The physicians replying to the questionnaire did not mention whether or not tangential fields were used. Treatments were given daily (excluding Sundays) or on alternate days. The total dosage varied from 1,000 to 3,500 r per field; one case was treated with 400 kv. for a total dose of 7,600 r to the axilla and scar. Palliative therapy was given to 3 ports, from 2,000 to 4,700 r per field. In a few cases radium needles or bombs were used. The axillae and cervical lymph nodes were treated by external irradiation in a palliative manner.

POSTMORTEM STUDIES

Postmortem examinations were done in 11.7 per cent of our series. Seventeen additional cases were found in the literature. The predominant sites of metastases (Table VII) as given in the autopsy records were: lungs 62.5 per cent, ribs and axillae 29.17 per cent, pleura 33.33 per cent, spine 25 per cent, pelvis and generalized metastases 20.83 per cent each.

TABLE VII: POSTMORTEM FINDINGS IN CARCINOMA OF THE MALE BREAST

	Author's Series (24 cases) %	Literature (17 cases) %
Local recurrences	...	17.65
Skin	12.5	5.88
Edema, upper extremity	...	11.76
Lungs	62.5	35.29
Pleura	33.3	17.65
Larynx	4.18	...
Mediastinal nodes	8.33	23.53
Ribs	29.17	5.88
Retroperitoneal lymph nodes	12.5	5.88
Mesenteric nodes	4.18	...
Inguinal nodes	4.18	5.88
Cervical nodes	4.18	5.88
Axilla	29.17	11.76
Liver	25.00	35.29
Spleen	8.33	...
Adrenal	8.33	...
Kidney	...	5.88
Pancreas	...	5.88
Stomach	...	5.88
Bladder	...	5.88
Spine	25.00	11.76
Clavicle	4.18	5.88
Pelvis	20.83	...
Skull	4.18	5.88
Generalized	20.83	11.76
Sternum	4.18	5.88
Brain	4.18	5.88
Thyroid	4.18	...

Intercurrent diseases were the cause of death of 4.4 per cent of the patients in our series: cardiac failure, endocarditis, arteriosclerosis, septicemia, diabetes, Bright's disease, and suicide being listed. No follow-up data were given in 3.9 per cent of the cases.

END RESULTS

In the past, statistics on end results have been calculated on a basis of the five-year survival rate. It is all too apparent that patients linger on for many years before dying of their disease and according to the present methods would be included in the five-year survival group. In this series the cases have been divided into three groups: (1) dead, (2) living, with recurrences or metastasis; (3) living and well (free of any metastasis). The series of Wainwright (61, 62), 1927 and 1930, Gilbert (19), Mülleder (41), and Lane-Claypon (32) are charted in a similar fashion for comparison (Table VIII).

TABLE VIII: END RESULTS IN CARCINOMA OF THE MALE BREAST

	Author's Series (205 cases) %			Wainwright (1927 Series) (111 cases) %		Wainwright (1930 Series) (41 cases) %			Gilbert (47 cases) %		Mülleder (12 cases) %	Lane-Claypon (Female) (2,006 cases) %
	D*	L†	LW‡	D	LW	D	L	LW	D	L	D	D
0–6 mos.	7.8	0.49	2.9	...	..	...	..	...	17.02	2.12	...	...
7–12 mos.	3.9	0.98	5.9	...	..	...	..	...	14.89	10.64	...	...
13–18 mos.	0.49	..	0.98	...	..	4.87	..	...	14.89	4.26	...	...
19–24 mos.	3.4	..	4.8	...	..	2.43	..	...	4.26	...	25.00	...
25–36 mos.	4.8	0.49	1.46	Aver. 33 mos.		2.43	..	...	10.68	6.38	...	...
37–48 mos.	2.44	..	2.44	...	..	2.43	..	9.75	...	...	8.33	80.00
49–60 mos.	1.96	1.46	0.98	...	..	4.87	..	9.75	4.26	...	16.66	...
5 years	**52.2**	..	..	**81.00**	**19.0**	**19.51**	..	...	**89.37**	**10.63**	**50.00**	**89.00**
6–10 years	3.9	1.46	7.3	12.35	..	12.19	2.43	31.71	4.26	6.38	8.33	11.00
11–15 years	2.9	..	2.9	4.75	..	...	..	2.43	...	...	...	...
16 years and up	2.9	..	2.44	1.9	..	...	..	2.43	...	...	...	...
No follow-up data	3.9	..	..	...	..	9.75	..	...	...	...	41.66	...

* D. Dead. † L. Living with recurrences or metastases. ‡ LW. Living and well, free of any recurrences or metastases.

In our series of 205 cases, 7.8 per cent died within the first six months, 11.7 per cent in the first year, 20.39 per cent within three years, and 52.2 per cent within five years; 2.9 per cent lived more than fifteen years. The patient surviving longest was still alive and well after twenty years. In one case recorded by Wainwright (61, 62) death occurred after twenty-two years, of heart disease; there was no evidence of carcinoma at the time of death. In Wainwright's 1927 series 81 per cent were dead within five years. Further follow-up, in 1930, of 41 patients who had been alive in 1927 revealed that 19.51 per cent of these had died within five years. Gilbert (19) reported 89.3 per cent, Mülleder (41) 50 per cent, and Lane-Claypon (32) (females) 89 per cent dead within five years.

SUMMARY AND CONCLUSIONS

(1) Two hundred and five cases of male breast carcinoma have been reviewed with follow-up data in 197. The longest follow-up period was twenty years, the shortest one week.

(2) Male breast cancer comprised 1.32 per cent of all breast cancers and 0.38 per cent of all cancers in males.

(3) The average age was 57.17 years; the youngest patient being twelve years and the oldest eighty-six years.

(4) The average time interval between tumor discovery and consultation with a physician was 1.14 years. Sixty-four per cent of the patients applied for treatment within one year after discovering the tumor and 90 per cent within two years.

(5) Symptoms were as follows: nipple retraction, 33.1 per cent; pain, 38.1 per cent; bleeding nipple, 14.6 per cent; ulceration, 20.6 per cent.

(6) There was a history of trauma in 23.9 per cent of the cases.

(7) The right breast was involved 99 times and the left 103; there were 3 instances of bilateral involvement.

(8) Male breast carcinoma is pathologically similar to carcinoma of the female breast, being predominantly of the adenocarcinomatous, scirrhous, and medullary types.

(9) Local recurrence was noted in 25 per cent of the cases. Of these, 25 per cent reported back to the physician within two years. There is no limit as to the length of time necessary for recurrence. Two recurrences occurred more than fifteen years after the original operation.

(10) Metastases were noted clinically in 46.34 per cent of the cases. Radiological evidence showed metastases to be chiefly osteolytic. The chief sites were: spine, pelvis, ribs, femur, and skull (Table VI).

(11) Pathological evidence of metas-

tasis was found in lungs, pleura, ribs, axilla, spine, and liver, including 24 of our cases and 17 from the literature.

(12) Surgery was performed in 65 per cent of our cases: 21 per cent had simple and 44 per cent had radical mastectomies.

(13) X-ray therapy was given in 53 per cent of the cases. Of this group, 23.8 per cent received preoperative, 55.1 per cent postoperative, and 21.1 per cent palliative therapy.

(14) Fifty-two per cent of the patients died within five years; 7.5 per cent were living and well; 7 per cent were living with recurrences from five to ten years; 3 per cent were living and well from ten to fifteen years; 2.9 per cent were living from sixteen to twenty years (Table VIII).

Prognosis in male breast cancer is poor. Fifty-two per cent of these patients died within five years in spite of adequate surgery and x-ray therapy in the majority of cases.

NOTE: The author is indebted to the following contributors for their excellent co-operation in collecting the above group of cases: Alameda County Hospital, California; A. D. Allen; V. W. Archer, University of Virginia Medical School; J. Aspray and A. Seeds; R. M. Bartlett; A. Bassler; R. Beeler; C. Brown; Buffalo City Hospital, New York; S. T. Cantril, Tumor Clinic, Swedish Hospital, Seattle, Washington; Carpenter Clinic, Delaware; M. Cassidy; J. J. Clark; J. R. Coffey; Columbus Cancer Clinic, Ohio; C. F. De Garis; R. DeBusk, St. Luke's Hospital, New York City; G. Dwinnel; W. Eastland; W. P. Elkins; L. H. Garland; L. B. Goldman; H. W. Grimm; W. C. Hall; W. Haworth and S. Rees; I. S. Hirsch; C. Henry, Tumor Clinic, Montreal General Hospital, Canada; Indianapolis City Hospital; T. Joyce; I. I. Kaplan, Division of Cancer, Bellevue Hospital, New York City; Keith, Keith and Shiflett; L. C. Kinney; C. Larson; E. Liljencrantz, Stanford University School of Medicine, San Francisco; M. Lenz; G. A. Mac Iver; A. B. McGraw; Massachusetts Memorial Hospital; F. C. Middleton, Saskatchewan Cancer Comm., Canada; A. W. Oughterson, Tumor Clinic, New Haven Hospital, Conn.; Paterson General Hospital, New Jersey; G. E. Pfahler; C. Phillips and C. A. Stevenson; Pondville Hospital, Massachusetts; U. Portmann; R. J. Reeves; San Francisco Hospital; K. W. Stenstrom and L. A. Titrud, University of Minnesota Medical School; R. S. Stone, University of California Medical School; J. M. Surver, Jefferson Hospital, Philadelphia; L. K. Sycamore; O. R. Trostler; Truesdale General Hospital, Massachusetts; A. Turnbull; United Hospital, New York; University of Oregon Medical School; U. S. Veterans Hospital, Hines, Illinois; F. J. Waas.

Station Hospital, Department of Radiology
Camp Callan, San Diego, Calif.

BIBLIOGRAPHY

1. ACHTERMANN, W.: Beiträge zur Klinik des Brustdrüsenkrebses beim Manne. Inaugural Dissertation, Köln, 1927.

2. ALBRIGHT, F., AUB, J. C., AND BAUER, W.: Hyperparathryoidism. J. A. M. A. **102:** 1276–1287, April 21, 1934.

3. ANDREWS, E., AND KAMPMEIER, O. F.: Swellings of the Male Breast. Surg., Gynec. & Obst. **44:** 30–38, January 1927.

4. AUGUSTINE, G.: Breast Tumors. J. Iowa M Soc. **28:** 8–10, January 1938.

5. BAILEY, H.: Studies in the Male Breast. Lancet **1:** 1258–1260, June 21, 1924.

6. BELL, W.: Scirrhous Carcinoma of the Male Breast. Brit. M. J. **1:** 363–364, 1903.

7. BERNS, A. W. C.: Ein Fall von Carcinoma mammae bei einem Manne. Arch. f. klin Chir. **35:** 228–230, 1887.

8. BLODGETT, A. N.: Cancer of Breast in a Child. Boston M. & S. J. **136:** 611, June 1897.

9. BORTIN, A., AND BOLTON, L. J.: Carcinoma of the Breast in the Male. M. J. & Rec. **133:** 230–233, March 4, 1931.

10. BRYAN, R.: Cancer of the Breast in a Boy Fifteen Years Old. Surg., Gynec. & Obst. **18:** 545–547, 1914.

11. CHEATLE, G. L., AND CUTLER, M.: Tumors of the Breast. Philadelphia, J. B. Lippincott Co., 1931, pp. 512–523.

12. COLEY, B. L.: Recurrent Carcinoma of the Male Breast. Am. J. Surg. **40:** 90–91, April 1926.

13. COOPER, A. B.: Anatomy and Diseases of the Breast. Philadelphia, Lea & Blanchard, 1845.

14. CUMSTON, C. G.: Cancer of the Male Breast. Internat. Clin. Ser. 30, **2:** 25–32, 1920.

15. DOWNS, E. E., AND HASTINGS, W. S.: Factors Influencing the Types of Metastatic Carcinoma of the Bone. Am. J. Roentgenol. **29:** 1–7, January 1933.

16. EWING, J.: Relation of Trauma to Malignant Tumors. Am. J. Surg. **40:** 30–35, February 1926.

17. FITSZWILLIAMS, D. C. L.: On the Breast. London, W. Heinemann, 1924.

18. GESCHICKTER, C. F., AND COPELAND, M. M.: Tumors of Bone, published by Am. J. Cancer, New York, 1931, pp. 476–551.

19. GILBERT, J. B.: Carcinoma of the Male Breast with Special Reference to Etiology. Surg., Gynec. & Obst. **57:** 451–466, October 1933.

20. GINSBURG, S.: Osteoplastic Skeletal Metastases from Carcinoma of the Breast. Arch. Surg. **11:** 219–236, 1925. Am. J. M. Sc. **171:** 520, 1926.

21. GUTMAN, A. B., TYSON, T. L., AND GUTMAN, E. B.: Serum Calcium, Inorganic Phosphorus, and Phosphatase Activity in Hyperparathyroidism, Paget's Disease, Multiple Myeloma and Neoplastic Disease of Bones. Arch. Int. Med. **57:** 379–413, February 1936.

22. HORSLEY, J. S., JR.: Benign and Malignant Lesions of the Male Breast. Ann. Surg. **109:** 912–920, June 1939.

23. JACOBS, A. W.: Skeletal and Pulmonary Metastases from Primary Carcinoma of the Breast. M. J. & Rec. **125:** 237–239, 1927.

24. JOLL, C. A.: Metastatic Tumors of Bone. Brit. J. Surg. **11:** 38–72, 1923–24.

25. JUDD, E. S., and MORSE, H. D. Carcinoma of

the Male Breast. Surg. Gynec. & Obst. **42:** 15–18, January 1926.

26. JUDD, E. S., AND SISTRUNK, W. E.: End Results in Operations for Cancer of the Breast. Surg., Gynec. & Obst. **18:** 289–294, March 1914.

27. KEYSER, C. R.: Five Cases of Carcinoma of the Male Breast. Lancet **1:** 1493–1495, May 28, 1904.

28. KNOX, L. C.: Trauma and Tumors. Arch. Path. **7:** 274–309, Feburary 1929.

29. KNOX, L. C.: Relationship of Massage to Metastasis in Malignant Tumors. Ann. Surg. **75:** 129–142, February 1922.

30. KUNATH, C. A.: Carcinoma of the Male Breast. J. Iowa M. Soc. **28:** 10–13, January 1938.

31. LACHMANN, E., AND WHELAN, M.: Roentgen Diagnosis of Osteoporosis and Its Limitations. Radiology **26:** 165–177, February 1936.

32. LANE-CLAYPON, J. E.: Report on the Late Results of Operation for Cancer of the Breast. British Ministry of Health, Report on Public Health and Medical Subjects No. 51, 1928.

33. LEDDY, E. T.: Roentgen Treatment of Metastasis to the Vertebrae and the Bones of the Pelvis from Carcinoma of the Breast. Am. J. Roentgenol. **24:** 657–672, December 1930.

34. LEWIS, D., AND RIENHOFF, W. F., JR.: A Study of the Results of Operation for the Cure of Cancer of the Breast. Ann. Surg. **95:** 336–400, March 1932.

35. LUDLOW, A. I.: Carcinoma of the Male Breast: Report of a Case in a Korean. China M. J. **39:** 1076–1079, 1925.

36. LUNN, J. R.: A Case of Cancer of the Breast in a Man Aged 91. Trans. Path. Soc., London **48:** 247, 1896–97.

37. MEYERDING, H. W., CARMAN, R. D., AND GARVIN, J. D.: Metastases from Carcinoma of the Breast; A Roentgenological Study. Radiology **5:** 486–488, December 1925.

38. MOORE, A. B.: Roentgenological Study of Metastatic Malignancy of the Bones. Am. J. Roentgenol. **6:** 588–594, December 1919.

39. MOORE, J. T.: Carcinoma and Other Tumors of the Male Breast. Am. J. Surg. **24:** 305–316, May 1934.

40. MOUSTARDIER, G.: Two Cases of Cancer of the Male Breast in Natives of Madagascar. Bull. Assoc. franç. p. l'étude du cancer **27:** 226–238, 1938. Abst. in Am. J. Cancer **34:** 469, 1938.

41. MÜLLEDER, A.: Zur Kasuistik der Mammacarcinome bei Männern. Arch. f. klin. Chir. **120:** 686–695, May 1922.

42. MURPHY, J. B.: Carcinoma of Male Breast. Surg. Clin. **3:** 569–574, 1914.

43. NEAL, M. P.: Malignant Tumors of the Male Breast. South. M. J. **25:** 841–844, August 1932.

44. NEAL, M. P., AND ROBNETT, D. A.: Generalized Osseous Metastasis Secondary to Atrophic Scirrhous Carcinoma of the Left Breast. Arch. Surg. **14:** 529–541, February 1927.

45. NEAL, M. P., AND SIMPSON, B. T.: Diseases of the Male Breast. J. Missouri M. A. **27:** 565–570, December 1930.

46. PFAHLER, G.: Roentgen Diagnosis of Metastatic Malignant Diseases of the Bone with Special Reference to the Spinal Column. Am. J. Roentgenol. **4:** 114–122, March 1917.

47. RIEHL, G., JR.: Über seltene Lokalisation von Metastasen des Mammacarcinoms. Arch. f. klin. Chir. **140:** 320–325, 1926.

48. ROBISON, R.: The Possible Significance of Hexosephosphoric Esters in Ossification. Biochem. J. **17:** 286–293, 1923.

49. ROSH, R.: Cancer of Breast in the Male. Am. J. Surg. **13:** 514–517, September 1931.

50. SARNOFF, J.: Cancer of the Breast in the Male. Surgery **3:** 766–773, May 1938.

51. SCHREINER, B. F.: Tumors of the Male Breast, Based on a Study of Thirty-one Cases. Radiology **18:** 90–92, January 1932.

52. SCHUCHARDT, B.: Weitere Mitteilung zur Kasuistik und Statistik der Neubildungen in der männlichen Brust. Arch f. klin Chir. **32:** 277–322, 1885.

53. SCHUCHARDT, B.: Ein Weitere Fall von Krebs der männlichen Brustdrüse. Arch. f. klin. Chir. **35:** 230–233, 1887.

54. SCHUCHARDT, B.: Weitere Mitteilung zur Kasuistik und Statistik d. Neubildungen d. männlichen Brust. Arch. f. klin. Chir. **41:** 64–100, 1890–91.

55. WARREN, SHIELDS, AND WITHAM, E. M.: Studies on Tumor Metastases: Distribution of Metastases in Cancer of the Breast. Surg. Gynec. & Obst. **57:** 81–85, July 1933.

56. SNOW, H.: Insidious Marrow Lesions of Mammary Carcinoma. Brit. M. J. **1:** 548–551, March 12, 1892.

57. SNURE, H., AND MANER, G. D.: Roentgen-Ray Evidence of Metastatic Malignancy in Bone. Radiology **28:** 172–177, February 1937.

58. SPEED, K.: Tumors of the Male Breast. Ann. Surg. **82:** 45–62, 1925.

59. STEWART, W. H.: Discussion of Paper by Moore (38)

60. VON RECKLINGHAUSEN, F.: Die Fibröse oder deformierende Osteitis. die Osteomalacie und die osteoplastische Carcinose, in ihren gegenseitigen Beziehungen. Festschr. f. R. Virchow, 1891, pp. 1–89.

61. WAINWRIGHT, J. M.: Carcinoma of the Male Breast. Arch. Surg. **14:** 836–860, 1927.

62. WAINWRIGHT, J. M.: Carcinoma of the Male Breast. Arch. Surg. **20:** 173–174. 1930.

63. WARFIELD, L. M.: Ca inoma of the Male Breast. Bull. Johns Hopkin Hosp. **12:** 305–310, October 1901.

64. WILLIAMS, W.: Duration of Life in Cancer of the Breast. Lancet, **1:** 72, 1889.

65. WOODARD, H. Q., AND HIGINBOTHAM, N. L.: Correlation between Serum Phosphatase and Roentgenographic Type in Bone Disease. Am. J. Cancer **31:** 221–237, October 1937.

66. YAMAMOTO, H.: Klinisch-statistischer Beitrag zur Kenntnis des Carcinoms des männlichen Brustdrüse. Dissertation, Rostock, 1911.

DISCUSSION

Harry L. Farmer, M.D. (Cleveland, Ohio): For every carcinoma of the breast in the male there are approximately 100 carcinomas of the breast in the female. The rarity of mammary cancer is to be expected because the male breast is not subjected to lactation, it does not undergo the recurrent monthly physiological disturbances of active menstrual life, and above all it is not subjected to the menopause.

The literature on this subject gives the impression that trauma is a definite etiologic factor in cancer of the male breast. If, however, the criteria set forth by Ewing are accepted, it is doubtful if trauma is by any means as significant a factor as observers would lead us to believe.

Malignant tumors in the male breast outnumber benign tumors in the ratio of almost 10 to 1. Benign lesions, particularly adenofibroma in old men, may be accompanied by retraction of the nipple and fixation to the surrounding tissues. Unless the diagnosis of carcinoma can be established, frozen section study of the excised tumor during the operation should be done before a radical operation is performed.

Oral Carcinoma[1]

WILLIAM E. HOWES, M.D., Visiting Radiation Therapist
LOUIS BERNSTEIN, M.D., Clinical Assistant Visiting Surgeon
Brooklyn Cancer Institute[2]

THE MOUTH IS composed of a highly specialized group of structures whose component parts are situated in close approximation to each other. The epithelium or oral mucous membrane is of the stratified squamous type and covers all of the intra-oral surfaces. This mucosa is stretched taut over the bone in the region of the hard palate and the alveolar ridges; it comes in close contact with muscle over the soft palate, tongue, and buccal surfaces; it lies in intimate relationship with a considerable amount of lymphoid tissue over the posterior surface of the tongue, tonsils, and lateral pharyngeal walls. The blood supply to and the lymphatic flow from the tongue and floor of the mouth are unusually rich. The close association of the mucosal surfaces with muscle, bone, blood vessel, and nerve, is a source of many difficulties and complications which the surgeon and radiotherapist must meet in treating intra-oral carcinoma.

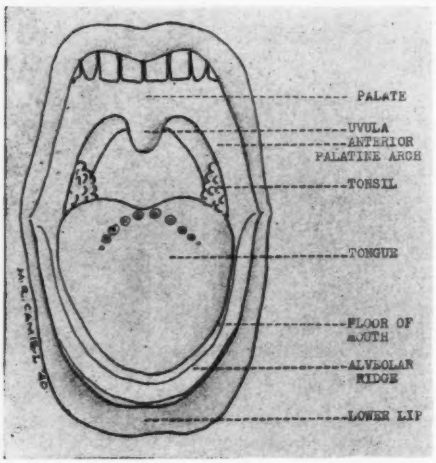

Fig. 1. Schematic drawing of intra-oral structures.

HISTOLOGY

The pathological classification of oral carcinomas at the Brooklyn Cancer Institute divides the tumors, which are almost always of squamous-cell origin, into four groups, depending on the degree of differentiation of the cells:

I. Intra-epidermal epithelioma, where criteria of malignancy are present but confined to the epithelium.
II. Prickle-cell type, where an organoid structure, intercellular bridges, and areas of keratinization are evident.
III. Transitional-cell type, where the cells are of large size, tend to have clear cytoplasm, lack intercellular bridges, and show no keratinization. Lympho-epithelioma is included in this group.
IV. Anaplastic type, where the cells are undifferentiated and lack definite arrangement.

Rare types are the basal-cell and the spindle, sarcoma-like varieties. We do not attempt to grade the tumor for an index of its radiosensitivity from the histologic picture alone. Other important factors in determining this index are the size of the tumor, its location in relation to the structures of the oral cavity, as bone, its tendency to ulcerate or fungate, and the presence of infection. The higher-grade, more sensitive tumors are more common in the posterior part of the oral cavity.

SYMPTOMATOLOGY

Pain is the usual impelling force that brings these patients to the physician.

[1] Read before the Radiological Society of North America at the Twenty-sixth Annual Meeting, Cleveland, Ohio, Dec. 2–6, 1940.
[2] Maurice Lenz, M.D., Director, Division of Cancer, Department of Hospitals, New York City.

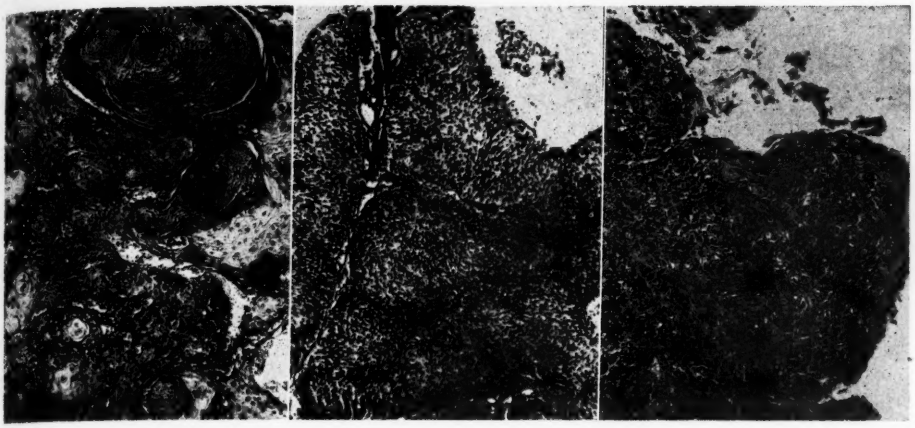

Fig. 2. Pathologic types of intra-oral carcinoma. Left: Prickle-cell carcinoma of anterior tongue. Center: Transitional-cell carcinoma of posterior tongue. Right: Anaplastic epidermoid carcinoma of tonsillar area.

This pain is secondary to ulceration and infection. The cases with pain as a presenting symptom without ulceration are the rare examples of extensive leukoplakia of the buccal mucosa or tongue, and the occasional case of glossitis secondary to gastrointestinal disease and vitamin deficiency. It has been the personal experience of the authors that these areas of leukoplakia can be present for years before breaking down into clinical carcinoma. As most of the symptoms are secondary to ulceration, infection, and metastatic spread to the chin and neck, further description is taken up under complications.

COMPLICATIONS AND THEIR TREATMENT

The mouth in its healthy state is a normal harbor of an immense bacterial flora, and with disease and ulceration, infection is always present. This infection makes the application of intensive irradiation a problem. When the necrotic areas reach the periosteum and involve the bone, the process becomes more resistant to therapeutic control and pain is accentuated. It has been our experience that it is preferable to remove all teeth in the field, as the peridental membrane leads directly into the depths of the alveolus and the secondary irradiation about the roots opens up the devitalized bone to infection. We have never attempted to amputate the crowns of the teeth as advocated by Martin (6). To remove a tooth during or after irradiation invites disaster. The procedure to control radiation osteitis is removal of the affected side of the mandible through the mouth, as described by Pack (8). To remove the mandible through an external approach frequently results in salivary fistula.

Hemorrhage must always be prevented, if possible, particularly when the ulceration extends into the lateral surface of the tongue and the floor of the mouth. It is wiser to ligate the affected artery (lingual, external carotid) prophylactically, to avoid bleeding.

Infection of any of the salivary glands, though frequently present, is seldom of sufficient severity to warrant more than local treatment. All enlarged lymph nodes in the submental, submaxillary, and cervical regions should be treated as metastases, unless proved otherwise. Metastatic spread of this nature is most common in carcinoma of the tongue and floor of the mouth, and should be included in any plan of treatment for such cases.

Syphilis may be a complication in carcinoma of the tongue. In its presence there are extensive changes throughout the mucosa, due to a generalized endarteritis, which causes delayed healing following sur-

TABLE I: ORAL CARCINOMA, SEX AND AGE INCIDENCE

Cases reviewed	138
Cases omitted	27
Cases included	111
Sex and Age Incidence	
Sex Incidence	
Females	8 (7.2%)
Males	103 (92.8%)
Age Incidence	
Average age	62
Youngest	32
Oldest	84
Age Groups	
30 to 39	3 (2.7%)
40 to 49	11 (10.0%)
50 to 59	27 (24.6%)
60 to 69	43 (38.2%)
70 to 79	23 (20.9%)
80 to 89	4 (3.6%)

gery or radiation. Antisyphilitic therapy should be given both during and after treatment.

Tuberculosis and other granulomata have not been found in association with oral carcinoma in our experience.

ETIOLOGY

The intrinsic causes of oral carcinoma are hereditary factors and anatomical defects plus pathological changes due to arteriosclerosis, syphilis, and vitamin deficiency. Common among extrinsic factors are areas of chronic irritation with infection, due to ill-fitting plates and other dentures, repeated injuries from sharp tooth fragments, reaction from the excessive use of tobacco and other irritants. Recently, the Plummer-Vinson syndrome has been cited as a possible etiological factor in the development of carcinoma.

GENERAL SURVEY

The series of cases reviewed here, numbering 138, includes all instances of oral carcinoma admitted to the Brooklyn Cancer Institute since October 1936; also those carried over to our present location,[3] but treated before that date. Twenty-seven cases have been omitted from the analyses because of insufficient data, lack of biopsy, history, or follow-up.

[3] The Brooklyn Cancer Institute moved to larger quarters in October 1936.

TABLE II: ORAL CARCINOMA, SITE OF LESION

	Number of Cases	Positive Serology
1. Tongue	49 (44.2%)	13 (26.5%)
2. Floor of mouth	16 (14.4%)	0
3. Alveolar ridge	7 (6.3%)	2 (28.5%)
4. Buccal mucosa	6 (5.4%)	2 (33.3%)
5. Palate	14 (12.6%)	0
6. Tonsillar area	19 (17.1%)	2 (10.5%)

Anatomical Classification: In Table II, the lesions are divided into six sub-groups, according to the location, and the incidence of syphilis for each is stated.

Clinical Classification: The cases have also been divided according to the extent of the lesion into the following clinical groups:

Stage I: A lesion 1.0 cm. or less in diameter and confined to its local anatomical structure.

Stage II: A lesion over 1.0 cm. in diameter, still confined to the local area.

Stage III: A lesion greater than 1.0 cm. in diameter, with local extension but no evidence of regional metastases, *i.e.*, from tonsil over onto soft palate, from tongue down onto floor of mouth.

Stage IV: A lesion greater than 1.0 cm. in diameter with local extension and regional lymph node involvement or with distant metastases.

In 1936 Schinz and Zuppinger (10) classified nasopharyngeal tumors on the basis of operability. This clinicopathological division has been followed in order to evaluate more completely the results of treatment, and to study further this group of cases in relation to prognosis and end results.

TABLE III: ORAL CARCINOMA, CLASSIFICATION OF LESIONS ACCORDING TO INVOLVEMENT

Stage I	1 case (0.9%)
Stage II	37 cases (33.3%)
Stage III	10 cases (9.0%)
Stage IV	63 cases (56.8%)

The low number of Stage III cases is explained by the fact that this stage probably represents a proportionately short time interval in the progress of the disease; when the carcinoma has once spread be-

yond its local environs there is likely to be lymphatic spread.

From the point of view of therapy such classification allows division of these cases into two main groups, namely, Stages I and II, where treatment should be directed with expectation of cure, the cases numbering 38 or 24.2 per cent of the total; Stages III and IV, consisting of 73 cases, or 65.8 per cent, where the extent of the pathology is such that treatment should be directed toward palliation or cure, but where palliation is all that can be reasonably expected.

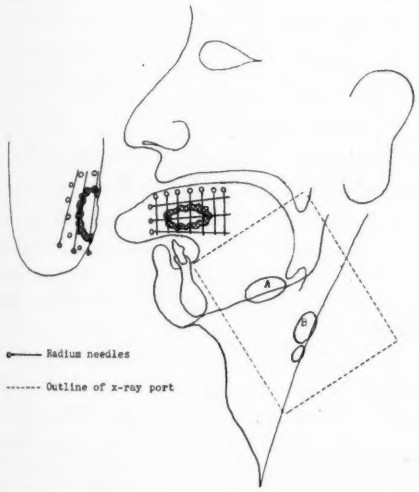

Fig. 3. Schematic drawing showing application of radiation in carcinoma of tongue. A. Lymph nodes of submaxillary triangle. B. Anterior cervical chain.

The entire group is made up of various types of patients such as are seen in any large metropolitan clinic. It consists of persons who are careless as to personal hygiene and in no sense introspective. The average duration of symptoms before seeking medical advice, however, was only 4.1 months. The shortness of this period is due partially to the association of pain with ulceration and infection. In spite of this short interval, 63 of the group represent Stage IV in our classification and 10 Stage III. In other words, the lesions are not of slow growth and low-grade malignancy, but are rapidly progressive tumors. It must be taken into consideration, also, that the history given dates back only to the presence of ulceration and pain. An estimated interval of two to twelve months before these lesions progress to ulceration should be added.

THERAPEUTIC RESULTS

The cases are grouped, treatment is outlined and end-results are given, according to the anatomical location of the lesion.

Tongue: Forty-nine cases, or 44.2 per cent of the whole, are listed in this largest group. The location was approximately evenly divided between the anterior and posterior portions of the tongue.

TABLE IV: CARCINOMA OF THE TONGUE

Anterior Half	
Clinical Classification	
Stage I	1 case
Stage II	11 cases
Stage III	2 cases
Stage IV	8 cases
Pathological Classification	
Prickle-cell	18 cases
Epidermoid	2 cases
Anaplastic	2 cases
Posterior Half	
Clinical Classification	
Stage I	0 cases
Stage II	3 cases
Stage III	5 cases
Stage IV	19 cases
Pathological Classification	
Prickle-cell	22 cases
Transitional	3 cases
Anaplastic	2 cases

It is generally agreed by Cade (1), Kaplan (5), Pack (8), and Stout (11) that oral carcinoma is primarily a radiation problem. Following institution of necessary oral hygiene, carcinoma of the tongue is usually treated in this clinic by inserting radium needles in mattress formation, the needles being so placed as to irradiate evenly both the lesion and an area at least 1.0 cm. beyond that which clinically appears involved. The needles are 27 and 35 mm. in length; each contains 2 mg. of radium element, or 0.8 mg. per centimeter of length for the shorter needle, and 0.57 mg. per centimeter in length for the longer

needle. The wall thickness of each needle is 0.5 mm. of platinum.

The dose given up to the present has been empirical and can be estimated as from 500 to 750 mg. hours per cubic centimeter. This dose per unit volume must be reduced when the lesion is large. Thus the average dose of interstitial radium for a tongue lesion will vary from 1,500 to 2,500 mg. hours. The low radium content in the needles allows them to be left *in situ* from 48 to 150 hours.

After the subsidence of the radiation reaction, x-ray therapy is instituted. Lateral ports are used, with the beam centered on the lesion. These ports are large enough to include the drainage areas of the submental and submaxillary regions, which usually requires an area 6 × 8 to 8 × 10 cm. The dose is 200 r in air to each area daily, until a total of 3,000 r in air has been delivered to each port. The total dose to be given depends usually on the extent of involvement, the type of individual, his skin sensitivity, the appearance of the mucous membrane, and the amount of infection present.

Following this treatment the patient is kept under careful surveillance. Any questionable node is considered an indication for radical neck dissection, provided the tongue lesion appears to be controlled and there is no evidence of distant metastases (Duffy, 4). The incidence of lymphatic metastases from carcinoma of the tongue has been reported as 66.7 per cent by Stout (11) and 75 per cent by Cutler and Buschke (3). Sachs (9) states that the incidence of distant metastases is far greater than the literature would indicate.

Local dissection of any involved lymph node must not be thought of as of curative value. It may be done for diagnosis, when radium in the form of seeds can be distributed through the area or radium tubes dropped into the bed. This interstitial radiation should be supplemented by external x-ray therapy. The skin tolerance is always greater when the external irradiation is given first.

Eight of the 49 cases reviewed, or 16.3 per cent, are clinically controlled up to the time of writing. If the 34 cases of Stages III and IV (Table IV), in which only palliation could be expected, are eliminated a more satisfactory end-result is obtained, namely, 8 out of 15 cases (Groups I and II) clinically controlled, which represents a salvage of 50 per cent.

Of those surviving, with the disease controlled, 1 is living less than one year; 1 is living more than one year but less than two years; 4 are living over two years; 1 is living three and a half years; 1 is living seven years. Two patients in whom control was obtained died of intercurrent disease, one year and four months and eight and a half years after treatment. Seven patients are living with carcinoma: 3, six months to one year; 1, a year; 2, approximately two years; 1, over four years.

Thirty-two patients died with the lesion uncontrolled. The immediate cause of death in these cases was apparently further extension of the carcinoma, plus infection, toxic absorption, poor nutrition, hemorrhage, and terminal bronchial pneumonia.

Floor of the Mouth: The prognosis in epitheliomata arising from the floor of the mouth is poor. No patient has applied to this cancer clinic before ulceration had taken place. The lesions are therefore not seen early and, even though a large area of epithelial surface may not be involved, there is often local lymphatic permeation at the time of the first examination. Furthermore, the floor of the mouth, as described by Martin and Sugarbaker (6), presents a blind pouch bounded laterally by the alveolar border and mesially by the reflection of the mucous membrane to the under surface of the tongue, making surgical drainage of this area poor. Thus necrosis, ulceration, and bleeding form a perfect media for the growth of pathogenic organisms and complicate radiation therapy.

Sixteen cases in this series are listed as arising from the floor of the mouth and are classified as follows: Stage II, 6 cases; Stage IV, 10 cases. Pathologically 14

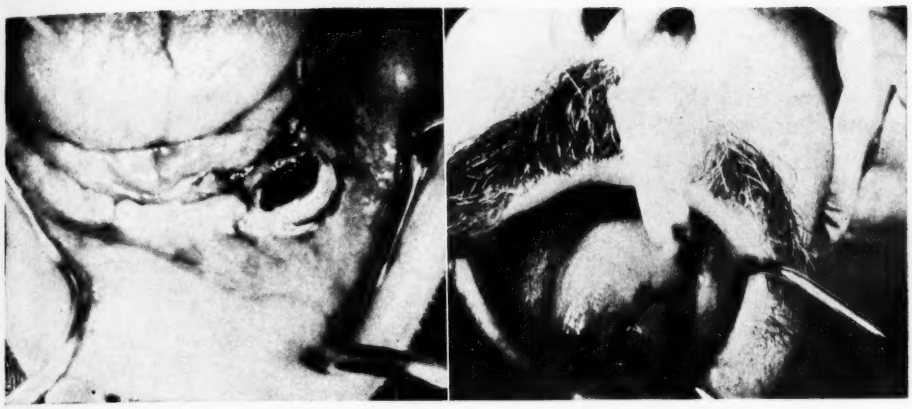

Fig. 4. Carcinoma of the floor of the mouth in a man of sixty-seven, before and after irradiation.

were of the prickle-cell type, 1 epidermoid, and 1 basal-cell.

The use of a radium mold in cases of this group has been discarded because of resulting injury to surrounding structures, as the mandible and tongue. Radium needles and seeds are used only after x-ray therapy has been delivered. Here again it is difficult to give a sufficient curative dose without severely injuring adjacent bone or soft tissues, allowing spread of infection.

The cases in the present series were treated with external radiation only. The following factors were used: 200 kv., 50 cm. S. T. D., 0.5 mm. Cu and 1.0 mm. Al filtration, 200 r in air delivered daily through two ports 6 × 8 cm., cross-firing the floor of the mouth and the adjacent lymphatic areas, until a total dose of 2000 r had been reached. Lymphatic spread, if present, was treated by the insertion of needles through the submental region. The results obtained with this type of treatment are listed below.

With the addition of the Chaoul type of x-ray apparatus to our armamentarium, the most satisfactory end-results have been obtained with so-called contact therapy. Here the depth dose is minimal, not over 25 per cent at the first centimeter; thus the maximum absorption is within the tumor and not the mandible. The dose is 1000 r daily, with a total surface dose of from 10,000 to 20,000 r units. This is supplemented by cross-firing the floor of the mouth either through lateral ports when the lesion is anterior, or anterior and posterior oblique ports when the site is further posterior. The factors used in the external beam are: 200 kv., half value layer 1.8 mm. Cu, 30 cm. S. T. D. when possible, approximately 50 r per minute, area 6 × 8 cm., total 200 r in air per field per day, for a total up to 3000 r to each area. This will result in a moderate to severe skin and mucous membrane reaction. Lymph node involvement is watched for, as with tongue lesions, and dealt with similarly.

Only 2 of the 16 patients treated are now alive with lesions controlled. Both of these have been observed for over four years. Two other patients were considered as having their lesion controlled, but have since died of intercurrent disease, three years after therapy. Three patients are alive, one year, eighteen months, and two years, respectively, with their disease still present.

Nine have died as follows: 5 in one year or less, 2 after eighteen months, 2 after two years.

Treatment of a more recent series with contact x-ray therapy appears to be giving more encouraging results.

Alveolar Ridge: As in the floor of the mouth, poor fitting dentures and chronic infection appear to be the most common etiological factors in carcinoma of the

alveolar ridge. These lesions commonly arise on the alveolar ridge in its middle or posterior third. The location is limited to the lower jaw in this series of 7 cases. Clinically 1 case was of Stage II and 6 were of Stage IV. Six were prickle-cell carcinomas and 1 epidermoid.

The treatment is the same as that described under carcinoma of the floor of the mouth. All 7 patients died, 4 in one year or less; 1 within eighteen months; 1 in two years; 1 in two and a half years.

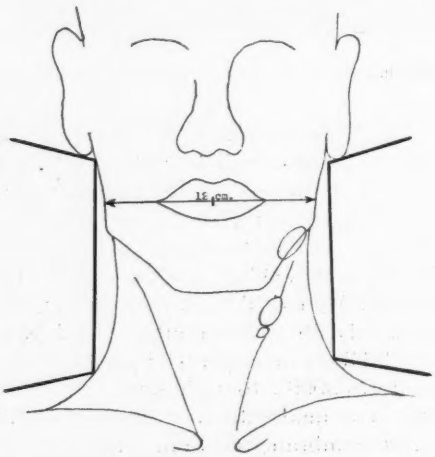

Fig. 5. Schematic drawing showing location of lateral x-ray ports and location of regional lymph nodes in usual intra-oral lesions. Treatment factors: 200 kv.; half-value layer 1.8 mm. copper; T. S. D. 50 cm.; field 6 × 8 cm. Depth dose 69 r at center per 127 r to skin.

BUCCAL MUCOSA

Lesions arising in the mucous membrane of the cheek appear to be similar to those arising from the floor of the mouth, being most difficult to control by any form of irradiation. The lesion is usually extensive, ulcerated, and infected. There is frequently evidence of extension to the cervical lymph nodes. Such a combination appears not to be amenable to our present methods of radiation therapy. Here again contact x-ray therapy appears to offer better results. All 6 cases in our series were of the prickle-cell type; 2 were of Stage II, 1 of Stage III, and 3 of Stage IV.

None of these patients survived. Four died within a year and the other 2 in eighteen months.

PALATE

Fourteen carcinomata of the palate have been treated and followed at the Brooklyn Cancer Institute. Nine of these cases were of Stage II, 1 of Stage III, and 4 of Stage IV. Pathologically 10 were prickle-cell carcinomas, 2 epidermoid carcinomas, 1 transitional, and 1 a mixed tumor.

Treatment has been irradiation. The most convenient approach is with the intra-oral cone with direct application of large doses of x-ray therapy, as described under lesions located in the floor of the mouth. This is followed by cross-firing through the cheeks externally with a more penetrating beam, with a half-value layer of at least 1.8 mm. Cu.

In contradistinction to the uniformly poor end-results in lesions of the floor of the mouth, 7 of our 14 patients with carcinomata of the palate are still living. Two are alive one and a half years but still have evidence of residual growth. Five appear clinically well eight months, one and a half years, two and a half years, three years, and nine years, respectively. Seven have died, 3 in one year or less; 1 in two years; 1 in two and a half years; 1 in three years; 1 in five years.

TONSILLAR REGION

Carcinoma of the tonsil cannot be ascribed to irritation and chronic infection. Usually the hyperplastic or cystic tonsil is not neoplastically involved, and syphilis with leukoplakia is usually not present. The lesion is often considered radiosensitive and Mattick (7) reports that three-year arrests may be expected in 35 to 40 per cent of early cases without metastases, and in 19 per cent of cases with metastases. Our observations do not corroborate these figures and Stout (11) reports even more discouraging results.

Of our 19 cases, 5 were of Stage II, 1 of Stage III, and 13 of Stage IV. Fourteen were of the prickle-cell type; 2 lymphoepitheliomata; 3 lymphosarcomata.

Irradiation is the treatment of choice. Here, again, direct application of the x-ray beam through an intra-oral cone is preferred, with cross-fire of the lesion through two or more external ports. These latter ports include the upper anterior cervical lymphatics. Any small residual lesion after such therapy or any recurrence can be attacked by inserting radon seeds into and about the lesion.

Only 3 of the 19 cases treated at the Brooklyn Cancer Institute appear to have been clinically controlled. Two of these cases have been followed less than two years and one just under one year. Another patient is alive, but with evidence of uncontrolled carcinoma, ten months following his first treatment.[4]

The remaining 15 patients have died of their disease: 8 in one year or less; 6 in eighteen months; 1 after three years.

SUMMARY

Our results emphasize the malignant nature of these intra-oral epitheliomata. In spite of the vigorous methods of radiation therapy utilized, a large percentage of these mucous membrane lesions are uncontrolled.

The number of cases in each subdivision and the percentage of survivals of over six months in each group are as follows:

Tongue	49 cases (16.3%)
Floor of the mouth	16 cases (14.4%)
Alveolar ridge	7 cases (6.3%)
Buccal mucosa	6 cases (5.4%)
Palate	14 cases (12.6%)
Tonsil	19 cases (17.1%)

This relatively poor showing can be ascribed to the fact that when first seen, 73 of 111 individuals were suffering from advanced disease. The largest percentage of survivals is in the earlier stages.

[4] In contradistinction to these end-results, one of us has had much more favorable results with a series seen in private practice.

CONCLUSIONS

Intra-oral carcinomata are actively developing new growths with early metastasis.

The poor end-results in intra-oral carcinoma are ascribed to: (1) the anatomical structure of the oral cavity and associated complications, as osteomyelitis, infection, hemorrhage, and early metastases; (2) age and type of individual. (3) the large percentage of advanced lesions.

These cases are entirely radiological problems except for care of complications.

Further intensive study is needed to improve methods of radiological attack.

152 Clinton St., Brooklyn, N. Y.

BIBLIOGRAPHY

1. CADE, S.: Cancer of the Tongue. Practitioner **143:** 40–48, July 1939.
2. CARLING, E. R.: Malignant Disease of Lips and Mouth. Practitioner **143:** 584–595, December 1939.
3. CUTLER, M., BUSCHKE, F., AND CANTRIL, S. T.: Cancer. Its Diagnosis and Treatment. Philadelphia, W. B. Saunders Co., 1938, pp. 104–143.
4. DUFFY, J. J.: Cervical Lymph Nodes in Intra-oral Carcinoma: Surgery or Irradiation? Am. J. Roentgenol. **39:** 767–777, May 1938.
5. KAPLAN, I. I.: Radiation Therapy of Malignancy of the Tongue. Amer. J. Surg. **30:** 227–233, November 1935.
6. MARTIN, H. E., AND SUGARBAKER, E. D.: Cancer of the Floor of the Mouth. Surg., Gynec. & Obst., **71:** 347–359, September 1940.
7. MATTICK, W. L.: Diagnosis and Treatment of Carcinoma of the Tonsil. Radiology **35:** 268–273, September 1940.
8. PACK, G. T., AND LIVINGSTON, E. M.: Treatment of Cancer and Allied Diseases. New York, Paul B. Hoeber, Inc., 1940.
9. SACHS, M. D.: Metastases from Carcinoma of the Tongue. Amer. J. Roentgenol. **42:** 833–842, December 1939.
10. SCHINZ, H. R., AND ZUPPINGER, A.: Zürcher Erfahrungen der Radiotherapie von bösartigen Nasopharynxgeschwülsten. Arch. f. klin. Chir. **187:** 582–613, 1937.
11. STOUT, A. P.: Human Cancer. Philadelphia, Lea and Febiger, 1932.

Depth Dose Calculation

Wherein Absorption in Unit Volume in the Depth, i.e., Volume Depth Dose, is the Index of Effective Radiation[1]

WILLIAM H. MEYER, M.D.

Director, Department of Radiology, N. Y. Post-Graduate Medical School and Hospital, Columbia University

A FORMER publication (1) has aroused sufficient interest to bring forth inquiries as to how the qualitative data there illustrated may be applied in the calculation of depth dosage, the author having advanced this method of depth dose calculation in preference to the various intensities indicated on isodose charts or the still less useful percentage depth dose at the 10th centimeter.

There is perhaps no gainsaying the fact that through any single portal the maximum absorption is always in the more superficial layers. Furthermore, the lower the voltage and weaker the filtration, the *greater is the absorption*, with the most intense biological effect *in the superficial layers*. When, therefore, in the treatment of superficial lesions a maximum radiation effect is desired, with the *least damage to deeper lying* tissues and a *minimum exit dose*, lower voltage and weaker filtration are the choice.[2]

To follow the same line of thought with regard to subcutaneous and more deeply seated lesions, the most logical method would be to select that quality, *i.e.*, voltage and filtration, whereby the lesion will, if possible, be encompassed within the zone of maximum absorption. This will of necessity be above the 50 per cent intensity level. When lesions are at a depth greater than that encompassed within the first half-value zone (this because of the limitation of the available equipment and technic), then the inclusion of the lesion within a zone of lesser absorption than the half value must suffice. In the treatment of deep-seated lesions in large persons, it stands without argument that (within reason) the highest available voltage with relatively strong filtration affords the maximum depth dosage. The first thing then is to determine the operating conditions under which the best quality factors are to be established.

By far the greatest number of therapy installations today are of 200 kv. capacity. There are a number of 400-kv. units and a very few operating at over 600 kv. One of the most frequently employed filters is 0.5 mm. copper faced with one or more millimeters of aluminum. From this, the filter thicknesses vary, with composite and other filters ranging from the equivalent of 0.25 mm. upward to 6.0 mm. and more of copper.

A survey of the literature backed by our own experimental work shows that the *half-value level*, or 50 per cent depth dose, in a large water phantom through a large portal, at the usual focal distance (50 to 70 cm.), varies from d/2 at 6 cm. with 200 kv. and 0.5 mm. Cu filter to d/2 at 9 cm. with 2.0 mm. Cu filter.[3]

There are a number of items, economic, physical, and physiological, which have a bearing on the quality factors to be employed. The experimental work thus far conducted and the clinical results obtained would hardly appear to justify the heavy expense of a 1,000,000 volt installation.[4]

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[1] Presented in connection with an exhibit at the Twenty-Fifth Annual Meeting of the Radiological Society of North America, Atlanta, Ga., Dec. 11–15, 1939.

[2] If a lesion is so located that protective backing can be employed, as in epithelioma of the lip, then strongly filtered radiation is feasible. Without such protective backing serious damage to the deeper lying tissues will result unless the proper radiation quality is applied.

[3] d/2, *i.e.*, the half-value level, is the depth at which 50 per cent of the measured surface intensity is recorded.

[4] In the light of present-day knowledge and experience, a top voltage of around 750 kv. with the equivalent of 6.0 to 8.0 mm. Cu filter will deliver a maximum depth dose of 50 per cent at about 10.5 cm. in a large water phantom.

It is also still an open question whether the radiation effectiveness with 400 kv. is superior to that attainable with 200 kv., since if an approximately *50 per cent longer focal* distance be employed with the latter (with the same filtration) but little difference in the half-value level or depth dose will be noted.

The necessity of the foregoing preamble arises from the variableness of the factors involved, influenced by individual opinion, the latter frequently based upon the limitation of the equipment and facilities available. It would appear best to avoid as far as possible minor controversial points and proceed with our method of evaluation of depth dosage, giving due consideration to the wide latitude of ray qualities existing under different operating conditions.

EXPERIMENTAL AND CLINICAL OBSERVATIONS

Of the many charts of ray qualities that are at hand, we have selected only one for illustrative purposes (Chart 1). The data on this chart were obtained from measurements in a large water phantom. The entrance portal was of medium large size, approximately 10 × 10 cm.; the quality factors, as indicated, were 200 kv. (constant potential), with 0.75 mm. Cu filter faced with 1.0 mm. Al, at a 50-cm. focal distance; the half-value level (measured in air) is d/2 = 17 mm. Al, or d/2 = 1.1 mm. Cu.[5] The abscissae, along the top of the chart, represent the per cent surface intensity. The ordinates (vertically along the left side) represent the centimeter depth in a water phantom.

Before proceeding with a more detailed analysis of this chart, a few remarks, both critical and constructive, as to further reasons for the presentation of this material may be acceptable. In our previous paper (1) we advanced a line of reasoning in criticism of the r dose as an index of bio-

[5] Our experience indicates that 0.75 mm. Cu filter affords a more practical working homogeneity of radiation with 200 kv. than the usually employed 0.5 mm. Cu, without too serious lengthening of the time factor.

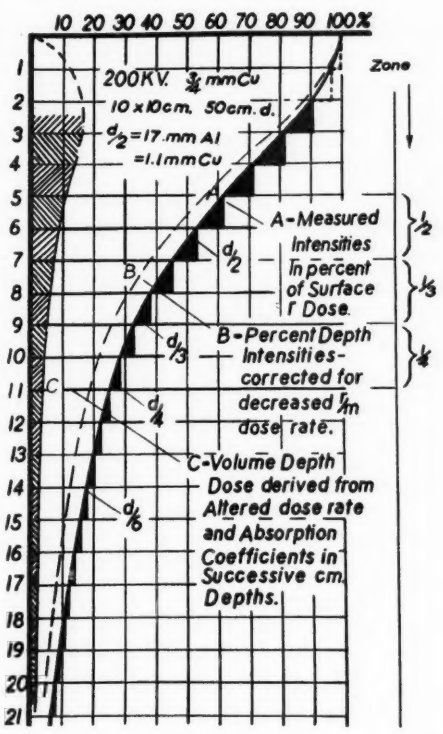


Chart 1. Volume depth dose: factors from which the data are derived.

Across the top, the abscissae represent the per cent intensity as measured by ionization. The figures arranged vertically on the left side show the cm. depth in a water phantom.

It must immediately be understood that this chart contains but a single set of dose factors of which there are innumerable variations. It therefore applies only to the specific factors here indicated. These are 200 kv. constant potential, 0.75 mm. Cu faced with 1.0 mm. Al, S.F.D. 50 cm., portal size 10 × 10 cm. d/2 (in air) = 17 mm. Al or 1.1 mm. Cu.

Curve A is derived from direct ionometric measurements in a water phantom, showing the measured intensities at successive depths. The triangular blocks represent the difference in incident and transmitted intensities in successive centimeters. The various half-value levels, d/2, d/4, etc., are indicated to the right of these blocks.

Curve B represents the calculated per cent of depth intensities corrected for the altered dose rate, since of necessity at the first half-value level, d/2, the r/m dose application must be one-half that at the surface. Likewise at d/4, the dose rate would be one-fourth that at the surface, etc.

Further correction for various absorption coefficients in successive centimeters has been applied in drawing curve C.

The shaded blocks along the left-hand side of the chart are illustrative of the effective absorption in successive cm. depths; this forms the key from which information with regard to volume depth dose is derived. For further details see text.

logical or *clinically observed reaction*, on the ground of the variability of this dose depending upon certain of the physical factors employed. The clinical deductions and physical conclusions we have drawn are based upon experiments as well as clinical observations of thousands of cases in over a quarter of a century in the radiation therapy department in this institution. It is only upon such volume of work that deductions such as have been drawn in this and correlated preceding articles are at all justifiable. A detailed description of isolated cases impresses us as a needless waste of space. Naturally, even a short synopsis of such a volume of material is impossible here. Suffice it to say that the records, charts, and data, along with statistical surveys, are on record and form the foundation of this presentation. A summary of the fundamentals upon which this material rests follows.

Quantitative: Surface dose calibrations are based on an epilation-erythema reaction, the experience including low-voltage, weak filtration scalp epilation, in cases of ringworm and favus, through intermediate to high-voltage and strong filtration in brain tumor cases, where complete epilation was again the determining surface dose factor. A dose of passive inhibitive action, *i.e.*, complete epilation followed by complete regrowth of hair on the scalp over a 10 × 10 cm. area forms our unit of surface reaction. This same dose will result in the majority of cases in a mild erythema on the more sensitive flexor surfaces of the body.

Through the years since 1915, various physical methods of calibration have been employed; in the early days, the pastille and photographic methods of Sabouraud, *et al.*, and Holzknecht, respectively; later the selenium cell of Fürstenau and the iontoquantimeter of Solomon and of Dessauer. Now, for some years the standardized ionization chambers of Wulf and Victoreen have been in use. The accuracy of the latter instruments has been controlled by a 50-mg. radium capsule preserved for this purpose.

All through the transitional period of changing from one physical intensity measure to another, clinical observations were supported by correlating the output of three different machines, maintaining a constancy of ma. on two meters supported by voltmeter, point, and sphere gap measurements; throughout the skin focal distance and portal size were fixed. Of major importance was the fact that the half-value layer as a quality measure was maintained throughout.

The significant outstanding fact remains that *the r dose is determined from reaction* and not the reverse, as some would seem to think. It is for this reason that with technical variations (later to be summarized) for a given reaction, as much as a 400 per cent variation in the r dose may be required.

Qualitative: The subject of quality determination of the x-rays was in the early days so uncertain that we soon realized the importance of uniformity at least, if not standardization, and appreciated the value of a fixed method. The necessity of this was the more important to us since in teaching we had to devise a method that would be comprehensible to those without much training in physics. By careful study and elimination, we concluded that the half-value method of quality determination, as originally suggested by Christen, affords the greatest accuracy and is most easily comprehensible. Fortunately, the half-value layer of quality determination forms the accepted international method today. The photographic method employing 2 Al scales, in 0.25- and 1.0-mm. steps, introduced by us more than twenty-five years ago (2), is still used by us for orientation and gross determination of the half-value layer of any and all qualities of radiation here employed. Naturally, the ionometric method for confirmation or correction has been added.

Irrespective of variations that may exist between the photographic and ionization methods, it is because of the constancy with which these half-value determinations

have here been made that we can duplicate the technic on any piece of equipment formerly employed or any new machines and technics that have been or may yet be instituted.

Without some means of correlating the foregoing physical data with clinically observed reactions, the whole would be of little use other than for the calibration of one machine or technic against another. It is for this reason that the epilation-erythema dose remains with us the surface unit dose standard, and from this point on, the attempt at dose determination is continued by the correlation of the physically measured half-value levels with absorption or unit volume depth dose in a water phantom.

From the clinical experience derived through the years of observation, and with the physico-technical support above described, the deductions herein incorporated have been drawn.

Vagaries of the r Dose: With respect to clinically observed reactions, the following statements may be made. (1) The r dose will vary considerably with the voltage or *filtration* employed. (2*a*) The r dose as measured in air will vary markedly with gross change in the *size* of the portal. (2*b*) Variations in the focal distance will also influence the depth dose. (3) There is again a wide difference in the reaction discernible depending upon the intensity of dose administration, meaning the *r per minute of dose application*, or the fractions or frequency of dose repetition. All of this leads to the reiterated conclusion that *the r dose is a physical measurement* and must be correlated with the foregoing factors before it becomes of practical application.

It should also be evident that the usual isodose measurements represent incident and transmitted intensities at given planes or levels and are not directly indicative of the biological effectiveness or true absorption.[6]

In our opinion, a ±10 per cent variation or error in the physically measured r dose would not be discernible by any of the present-day methods, including clinical, biological, and microscopic observations. Gross or round figures will be employed, therefore, so long as they remain within the ±10 per cent limits of experimental error.

In place of plane intensities, the author proposes to use mass absorption or, what is perhaps a better term, *volume depth dose*, as an index of radiation effectiveness.

Volume Depth Dose: Information as to volume depth dose is obtainable from absorption coefficients applied to small areas or segments of the curve. Gross variations in absorption coefficients are determinable by drawing secants at the various half-value levels. Another method which lends itself well for illustrative purposes is to observe the radiation lost in successive centimeter depths, as illustrated by the small wedge-shaped blocks drawn in successive centimeter depths along the transmission curve (Chart 1). These represent closely the difference between incident and transmitted intensity at successive centimeter depths.

Whereas an error occurs in the more superficial layers because of the difference in backscattering, this can have but little influence on the correctness of the interpretation in the depth, since there will be but little difference in the amount of backscattering in the neighboring centimeter units in the deeper layers. When, therefore, the error introduced by backscattering is practically constant, it may be presumed that the difference in incident and transmitted intensity of the primary beam is a fair index of radiation lost or absorbed at these depths.

With due consideration of the foregoing remarks, we return to a further analysis of the data presented in Chart 1.

In Chart 1, curve A represents the measured intensities through the middle of a large water phantom. The small wedge-shaped blocks along the right-hand side of the curve are merely illustrative of the

[6] In view of the uncertainties in mathematical gyrations introduced in some quarters, creating a confusing backscatter fog, let it be remembered that water *phantom measurements* are *inclusive* of *backscatter*.

radiation intensity lost in each succeeding centimeter depth, that is, the difference between the incident and transmitted intensity. (The difference between this and similar curves previously presented is that, whereas on former charts the exponential or ideal curve was illustrated, on this the actual measured intensities in a water phantom are recorded.)

The broken line B is derived from the measured intensities as recorded in curve A, corrected for the decrease in intensity rate or r/m of dose application at various depths.

The shaded blocks appearing along the left-hand side of the chart opposite the successive centimeter depths represent the per cent radiation effectiveness or volume depth dose in successive centimeters with all correction factors applied, including the absorption coefficient product as well as the altered rate of dose administration.

Between the levels indicated as d/2, d/4, and d/8, the one-third and one-sixth layers may be indicated as d/3 and d/6, respectively.

The brackets along the right-hand side of the chart encompass zones wherein the depth dose is indicated in fractions of a unit.

It is evident that absorption zones will increase or diminish in depth and extent as the penetration is increased or diminished, respectively. In this specific instance, *i.e.*, Chart 1, the radiation absorption effectiveness in the zone extending from approximately 5 to 7 cm. is one-half that of a similar more superficially located zone, within $\pm 10\%$ variation. One-third radiation absorption effectiveness extends in the zone from 7 to 9 cm. One-fourth value or 25 per cent extends from 9 to 11 cm., etc.

By way of practical application, it may be said that a lesion included within a specific zone has received the fraction of the unit dose indicated. When the size and depth of the lesion are such as to be included within two of the zones, then each part will have received the designated fraction. When, however, by cross-fire cumulation, a heavy depth dose is desired, it would appear better to accept the smaller fraction as the effective dose.

A study of the chart reveals that the dosage calculated by this method is not as great as that indicated at some levels of the average isodose chart. This is of importance from the standpoint of the number of portals required for cross-fire. Beyond the one-third or within the one-fourth depth dose zones, as much as a 50 per cent increase in the number of portals for cross-fire might be indicated as compared to the percentage depth dose derived from an isodose chart.

That the depth dose with regard to the position of the half-value levels and the extent of the several dose zones will also vary according to the voltage and filtration employed has already been mentioned (1). The problem at the moment has to do rather with variations in either a single isodose chart or the depth dosage as presented in Chart 1.

Though the voltage and filtration remain the same, there may be changes in the *size of the portal* or area irradiated, as well as changes in focal distance, which influence the depth dose. The data thus far analyzed are derived from measurements in a large phantom with portals of given dimensions as follows: a 14-cm. circle, a 12.5-cm. square, an oblong 10 X 15 cm. All of these have approximately the same area. (These areas were selected because they correspond most closely to frequently employed sizes and shapes, and allow sufficient latitude to cover a considerable number of routine cases as these present themselves.)

Influence of the Portal Size upon Depth Dose: Experimentally (see Chart 3) we have found that when the mean diameter of the portal, above given, is reduced to about one-half (which means a reduction to about one-fourth of the total area), the half-value level is one full centimeter less, thereby reducing the depth dose throughout as well as diminishing the size of the various absorption zones. Thus, if a circular area 14 cm. in diameter is re-

duced to 7 cm. in diameter, the first half-value or 50 per cent depth dose would move back from 6 cm. (Chart 3, curve *c*) to 5 cm. If the portal were again reduced from 7 to 3.5 cm. in diameter, the 50 per cent depth dose would move back to less than 4 cm. depth.

Just as these reductions in depth dose occur with reduction in size of the area irradiated, a converse change takes place with the same relative increase in the size of the portal. Thus, if because of the large size of the patient the area to be irradiated could be increased to double the size of the portal with which the data on the chart were obtained, the half-value level would be found to be about 1 cm. deeper than with the smaller area. The correction factors to be applied thus become evident. It is also clear that with every change in technic, a new depth dose chart would have to be devised to indicate the location and relative depth of each of the various absorption zones.

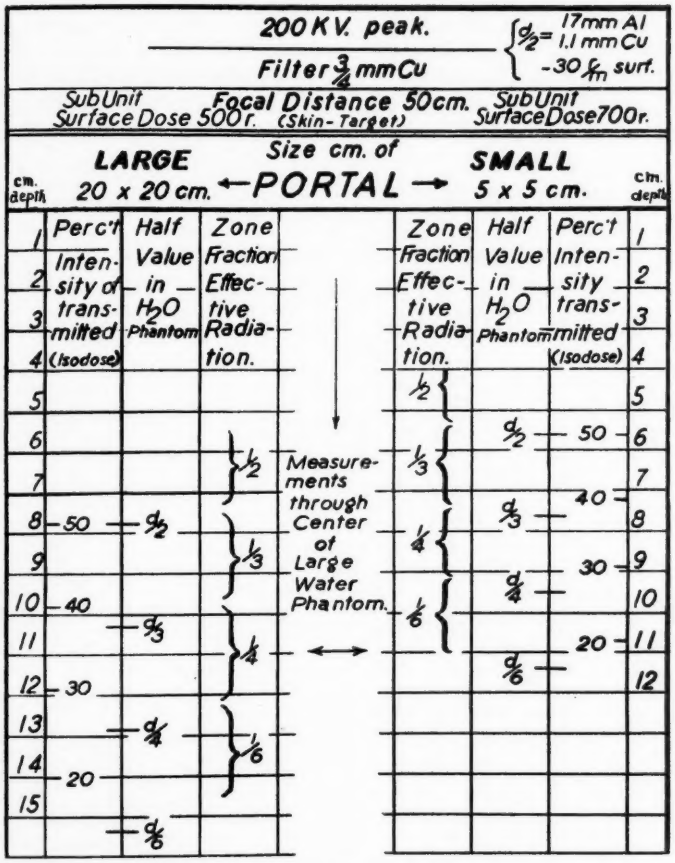


Chart 2. Influence of change in portal size on depth dose, other factors (kilovoltage, filtration, S.F.D.) remaining constant.

The data on the left- and right-hand sides of the chart represent the difference in depth dose with large and small portals 20 × 20 cm. and 5 × 5 cm., respectively. It will be noted, for example, by the volume depth dose or fraction effective radiation, that between the 10th and 11th cm. depth, one-fourth radiation effectiveness occurs with the large portal, whereas this is decreased to one-sixth effectiveness at the same depth with the small portal.

Focal Distance and Depth Dose: Experimentally (Chart 4) it has also been found

that marked changes in focal distance also result in a considerable variation in the depth dose. The shorter the focal distance, the less the depth dose; the longer the focal distance, the greater the depth dose. A decrease of more than 1 cm. in the depth dose with regard to the position of the first half-value level would result if the focal distance were cut from 50 to 25 cm. Conversely, an increase in the half-value depth dose of about 0.5 cm. would result with an increase in focal distance from 50 to 70 cm. These changes in depth dosage have been found to be practically applicable on a logarithmic basis, the result of experimental data with changes in portal size having been incorporated in Chart 4.

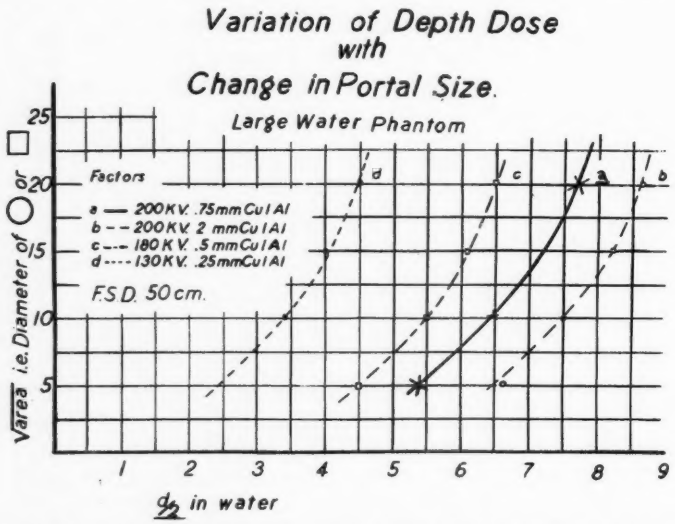


Chart 3. Change in depth dose resulting from alterations in the portal size. The figures along the left-hand side indicate the square root of the area; those along the bottom of the chart the half-value level in water in a large phantom. As a specific example, the data derived from curve (*a*) are incorporated in Chart 2, *i.e.*, with a large portal, 20 cm. in diameter, 50 per cent measured intensity occurs at 7.75 cm. depth, whereas with a 5-cm portal the 50 per cent dose is recorded at 5.25 cm. depth.

The 50 per cent depth dose can, of course, be found for areas of any other size on this curve. On curves (*b*), (*c*), and (*d*), the 50 per cent depth dose with other of the more frequently used technics can be determined. The clinical factors for the respective curves are indicated on the chart.

DISCUSSION

As experience accumulates with the lapse of time, the more certain is the author that the minor complexities of ray quality selection and designation should not deter one from the effort at solution; neither do the uncertainties involved excuse the recklessness with which technical variations are applied.

Irrespective of the conclusion drawn from some biological experimentation (namely, that the reaction with a given r dose is independent of the quality or wavelength), every radiologist of experience knows from clinical observations that the r dose varies with certain technical factors, the most important of which is filtration. The fact that some of the more recent biological experimentation supports this clinical impression appears to be lost.

So much has been published, from at least one source, about the treatment of cancer with 200 kv., 0.5 mm. Cu, at 50 cm. skin focal distance, that with at least nine out of ten radiologists this appears to form the basis or standard of their technic. This is in total disregard of the fact

that at this voltage, a far more practical working homogeneity, with but little increase in the time factor, is attained with 0.75 mm. Cu or more as a filter. I might supplement this with the statement that for deep-seated lesions, a filter equivalent to 2.0 mm. Cu has been found most desirable. There is too frequently a complete lack of correlation between the physical data and their practical application in clinical radiation therapy.

deeper tissues is necessary, so that the zone of *maximum absorption may be brought to bear upon the lesion site;* furthermore, there should be the *least possible damage to neighboring and deeper lying tissues and organs,* and finally *cross-fire efficiency* will be enhanced *with a minimal exit dose.* Only when these factors are reasonably well applied can radiation therapy be elevated from empiricism to reasonable scientific accuracy.

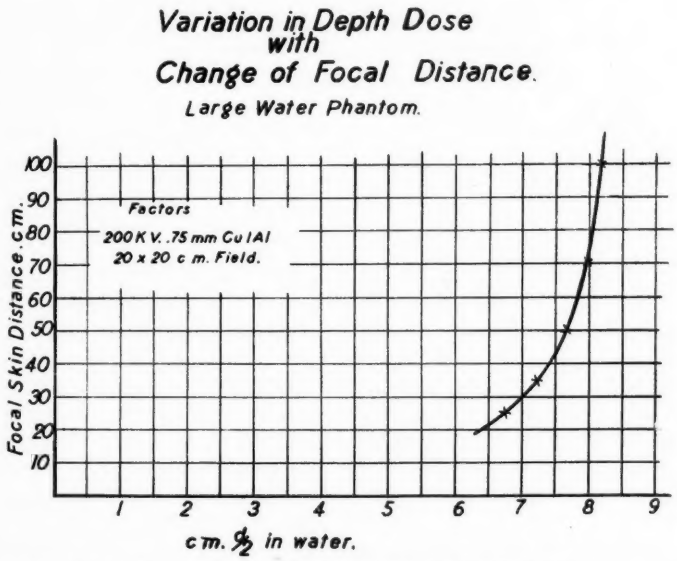


Chart 4. Influence of altered focal distance on the depth dose.
As in Chart 3, the abscissae indicate the half-value level in a water phantom. The skin focal distances up to 100 cm. are indicated on the left. The curve indicates an increasingly rapid decline of the depth dose with focal distances shorter than 50 cm. On the other hand, but a minimum improvement in the depth dose is indicated with focal distances greater than 70 cm.

In surveying the rather voluminous reports on radiation therapy in benign or inflammatory lesions with fractional or relatively small total dosage, the technical variations are such that the voltage and filter factors would appear of minor importance. If the reported cures (?) are true, this would bespeak the remarkable effectiveness of radiation therapy, but most certainly afford no scientific or reasonably accurate data upon which to depend. When heavy or maximum dosage to a lesion is required, then a reasonable knowledge of radiation effectiveness in the

True, the size, structure, and density of the various parts under treatment may have a considerable influence on the calculated depth dose; thus, the interposition of osseous structure may change the absorption equivalent to the ratio of 1 for each 2 cm. of the measured water phantom. Conversely, the air in the lung may extend the absorption readings to 4 cm. for each one in water.

Unfortunately because of such variables some, too clinically minded, literally disregard all physical dose measurements and calibration. Whether absorption in water

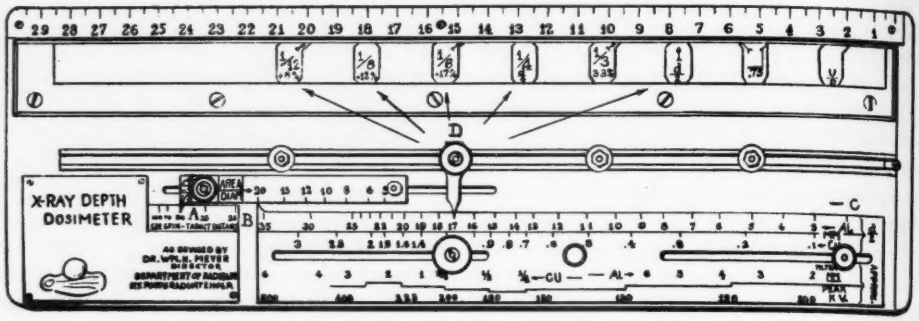


Fig. 1. Scale of author's depth dosimeter. The experimental data presented in this article have been incorporated in the scale. The instrument permits the rapid determination of depth dosage with innumerable variable factors, and covers a volume of isodose chart measurements.

A detailed study of the scale will reveal a latitude of skin focal distances of from 25 to 100 cm. (A). The square root of the area or diameter ranges from 5 to 20 cm. (B).

Though the approximate voltage and filter thickness are indicated at the bottom of the larger sliding scale, the accurate method of designating the quality is to determine the half-value layer in either Al or Cu; this appears along the top of the large scale (C).

When the pointers are properly set for the operating conditions employed, then the depth dose in either the successive half-value levels or zones of radiation efficiency can be read by the markers (D) opposite the cm. scale.

be absolutely the same as that in human tissue or not is utterly beside the point. This presentation seeks to point out that the possession of such knowledge affords a correlation of calibration data and measurements obtained in a water phantom, thereby establishing a reasonable working concept of depth dosage.

RECAPITULATION

In the preceding pages, we have attempted to show that radiation effectiveness is dependent upon volume depth dose and have presented a method of estimating and indicating the depth dose in fractions of a unit. The unit, of course, is based upon the r dose delivered at the surface. The fractions in the depth are in relation to a zone of similar thickness immediately below the surface and vary according to (*a*) voltage and filtration; (*b*) the size of the portal; (*c*) the depth in relation to the focal distance; (*d*) the r/m of dose application or fractionation.

In translating the transmitted radiation intensities into effective depth dosage, the correction factor for the altered rate of dose administration at various depths has thus been considered.

As an aid in solving the somewhat complicated mathematical factors involved, we have constructed a calibration instrument for the more rapid determination of the depth doses at various centimeters within the limits of the usual technical variations. The illustration given here (Fig. 1) merely shows the variable factors incorporated in the scale, the most important of which are variations in focal distance; required changes in the size of the portal; the operating conditions under which the half-value layers in Al or Cu are determined; and the relation of these to the dose obtained in the various centimeter depths of a water phantom. A more detailed description of the construction and operation of this calibration instrument will have to find place elsewhere.

Before concluding, I would reiterate that the surface unit dose is based upon numerous epilation-erythema reactions over a scale of radiation qualities ranging from 50 kv. and no filtration (other than the tube wall) to over 200 kv. and 2.0 mm. Cu filtration. The cases employed for correlating the physical and clinical data included, in the main, ringworm and favus, wherein epilation was obtained with low voltage and weak filtration. The data with respect to the epilation-erythema

reaction with high voltage and strong filtration, up to 2 mm. Cu, were derived from brain tumor cases. The r dose in this series varies from 350 r with weak filtration to 700 r with strong filtration. The correlation of the volume depth dose as here employed with depth dose reactions was established through such cases, in which the relative radiosensitivity of the lesions was reasonably well known.

Exclusive of benign and inflammatory lesions, the group of irradiated cases is as follows:

In verification of the variation of the r dose with respect to the size of the portal in the treatment of superficial lesions, we have some 255 cases of epithelioma, squamous-cell and mixed-cell types, ranging in size from 1 to 8 cm. diameter, successfully treated by the multi-unit dose method, with less than 2 per cent recurrence, within a minimum five-year follow-up period.

In support of our method of volume depth dose estimation, perhaps the most accurate information was obtained from the treatment of 100 consecutive cases in which the castration dose (checking of the menstrual function) by treatment of the ovaries, with various ray qualities according to our method of dose selection for the size and depth of the lesion or organ, was obtained. In order to avoid the complexities of cumulative dosage calculation by fractionation, these cases were all treated at a single sitting with the delivery of one third of the unit dose to the estimated depth or level of the ovary. The amenorrhea was complete and remained so for periods upward of five years.

Further cases in which the same method of dose estimation was employed include 189 lymphogranulomas, 82 lymphosarcomas, 15 mediastinal lymphoblastomas (?), 6 lympho-epitheliomas, 26 lymphatic and myelogenous leukemias (treatment limited to the enlarged spleens in the latter), 3 endothelial sarcomas, 34 embryonal carcinomas.

In all of these cases, the effort was made to bring the areas of tumefaction within the 50 per cent depth zone. When the lesion was beyond this depth, as nearly as possible a 50 per cent depth dose to the center of the lesion was delivered by cross-fire. The effort was also made to complete the treatment of any given area at one sitting. In widely disseminated lesions, a reasonable interval for observation and reaction was allowed before a second area was similarly irradiated.

Fig. 2. Epilation reaction. The pair of photographs herewith presented are purely illustrative of 100 consecutive cases of epilation with the technical variations as mentioned in the text.

The particular case here illustrated was one of brain tumor, with complete epilation three weeks after the completion of radiation therapy (left). The photograph on the right shows the same patient with a luxuriant regrowth three months later. It is upon such reaction that the unit surface dose is here standardized.

Note: The foregoing applies to non-toxic cases. It stands to reason that in the treatment of disease in general, each case must receive individual consideration. The methods above outlined are not applicable in more severely acute febrile cases, nor where the normal processes of elimination are impaired.

Neither is it to be presumed from the foregoing that the author does not recommend or use the fractional cumulative method of radiation therapy when indicated. As a matter of fact, by far the greater number of cases are at present being treated by the fractionation method. Since, however, this adds further complexities to the determination of the r dose, for any given reaction, it seemed best for standardization purposes to include here only those cases where radiation therapy in sufficiently strong dosage was administered at one sitting.

Finally, there was no intent in this presentation to enter upon a detailed description of the treatment of any specific disease or lesion. It will have been observed that but little if any mention of cancer as such (excepting epithelioma) has appeared in this communication. The reason is that the author has included in his discussion only lesions in which he believes radiation therapy to be indicated definitely,

and though some beneficial effects may have been noted, and some cancer patients statistically reported as alive at the end of a five-year period, nevertheless there is a serious doubt as to whether any deep-seated scirrhous, cystic, or adenocarcinomatous lesion has ever been cured by radiation.

The author desires to express his appreciation of the co-operation of members of the medical staff at the N. Y. Post-Graduate Medical School and Hospital, as well as of the technical assistance in the Department of Radiology. He is particularly grateful to Dr. Arthur Mutscheller for his almost limitless patience in carrying out the necessary experiments and preparing the charts and data.

303 E. 20th St., New York, N. Y.

REFERENCES

1. MEYER, WM. H.: Co-Relation of Physical and Clinical Data in Radiation Therapy. Radiology 32: 23–45, January 1939. (Includes bibliography.)

2. MEYER, WM. H.: Measurement of Roentgen Ray Quality by Means of the Photographic Determination of the Half Value Layer. Am. J. Roentgenol. 16: 26–29, July 1926.

Cerebral Arteriography with Diodrast, Fifty Per Cent[1]

SIDNEY W. GROSS, M.D.

New York

CEREBRAL arteriography was introduced by Moniz in 1927 (1). After experimenting with several radio-opaque substances he chose a colloidal preparation of thorium dioxide, thorotrast, as the most suitable. The objections and potential dangers in the use of this drug have been repeatedly pointed out (2).

Diodrast (3,4-diiodo-4-pyridon-*N*-acetic acid diethanolamine) has been used for many years for intravenous pyelography and more recently for the visualization of the chambers of the heart and great blood vessels (3). Experiences with the use of diodrast for the visualization of the cerebral circulation of the dog and in man have been reported (4). At first a solution of 70 per cent diodrast was injected into the common carotid artery. Three of 12 patients so injected, however, developed jacksonian seizures immediately following the injection. Following this, 35 per cent diodrast, which is available commercially, was used, but adequate visualization of the cerebral circulation was not obtained in every case. When the concentration was raised to 50 per cent uniformly good visualization was obtained and no serious reactions have occurred thus far. The technic employed at the present time is as follows:

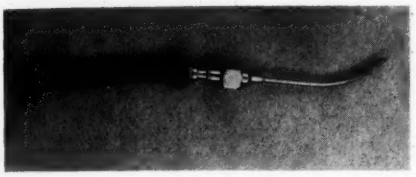


Fig. 1. Cannula with rubber tube connection.

(1) The patient is prepared by the administration of 5 grains of sodium phenobarbital an hour before the injection.

(2) The common carotid artery on the side of the suspected lesion is exposed under local anesthesia by a small incision parallel to the clavicle and about an inch above it. A narrow vaseline tape is passed under the common carotid artery to isolate it from the surrounding structures.

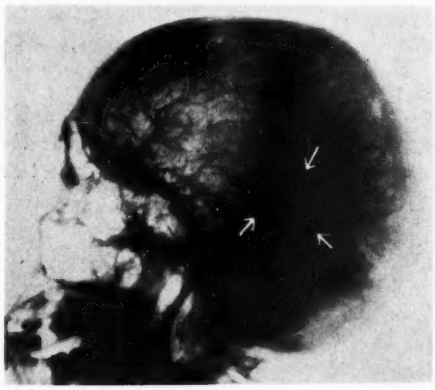


Fig. 2. Diodrast (50 per cent) arteriogram, showing temporo-parietal glioma.

(3) The patient's head is placed in position for a lateral x-ray photograph. An x-ray film is placed in proper position and all preparations are made to obtain a rapid exposure.

(4) The common carotid artery is then punctured with a curved 17-gauge needle having a rubber connection (Fig. 1).

(5) A syringe containing 15 c.c. of 50 per cent diodrast solution is attached to the rubber connection and after ensuring that the needle is within the lumen of the artery by permitting a few cubic centimeters of blood to run into the syringe, 10 to 12 c.c. of the solution is injected as rapidly as possible and the film exposed during the injection. The exposure should not require more than a quarter of a second.

[1] From the Department of Neurology and Neurosurgery and the Department of Radiology of the Mount Sinai Hospital. Accepted for publication in October 1940.

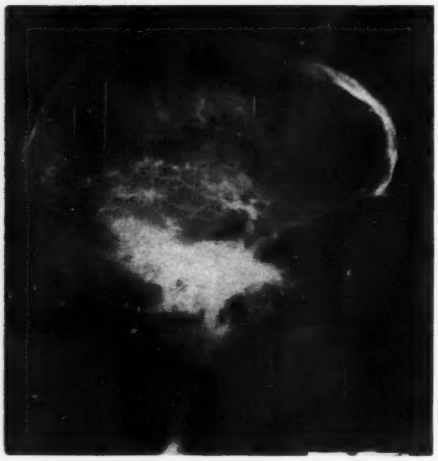


Fig. 3. Diodrast (50 per cent) arteriogram, showing aneurysm of circle of Willis.

If stereoscopic views are desired or if the first film proves unsatisfactory, while the needle is still in place a second injection may be carried out.

(6) Bleeding from the puncture wound in the artery usually stops as soon as the needle is withdrawn. Occasionally, however, pressure with a sponge soaked in warm saline may be required for a few minutes. The wound is then closed with a few interrupted silk sutures.

Figures 2 and 3 are reproductions of arteriograms obtained by the injection of 50 per cent diodrast solution into the common carotid artery.

8 East 83rd St., New York, N. Y.

REFERENCES

1. EGAS MONIZ: L'angiographie cérébrale, Paris, Masson et Cie, 1934.
2. Editorial, J. A. M. A. **108:** 1656, 1937.
3. ROBB, G. P., AND STEINBERG, I.: Visualization of Chambers of Heart, Pulmonary Circulation, and Great Blood Vessels in Man, Am. J. Roentgenol. **41:** 1–17, 1939.
4. GROSS, S. W.: Cerebral Arteriography in the Dog and in Man with a Rapidly Excreted Organic Iodide, Proc. Soc. Exper. Biol. & Med. **42:** 258–259 1939. Arch. Neurol. & Psychiat. **44:** 217, 1940.

Rhomboid Depression of the Clavicle[1]

SIMON SHULMAN, M.D.

Roentgenologist, St. Joseph's Hospital, Far Rockaway, N. Y.

THE PURPOSE OF this communication is to call attention to the presence of a normal anatomical landmark of the clavicle which is ordinarily not visible on the roentgenogram but which, in rare instances, may be so well developed as to simulate and be confused with a destructive bone lesion. The importance of differentiating such an anomaly from the various pathological conditions which are known to involve the same region, as osteomyelitis, tuberculosis, syphilis, and malignant neoplasms, cannot be disputed. A comprehensive survey of the American literature has disclosed only a single reference to the possible occurrence of an anomaly of this character (1).

The normal anatomy of the clavicle is too well known to warrant repetition. A brief description, however, of the region under discussion appears to be in order. According to Gray's *Anatomy*, on the medial part of the inferior or subclavian surface there is a rough, broad area, the costal tuberosity or rhomboid depression, rather more than 2 cm. in length, for the attachment of the costoclavicular ligament, which passes from the rhomboid depression of the clavicle to the cartilage of the first rib. In the average person, the rhomboid depression is too shallow to be visualized roentgenographically. Occasionally the existence of the usual shallow depression can be detected as a very slight indentation on the inferior margin of the inner end of the clavicle. Rarely, the depression may be very deep and penetrate about half-way through the thickness of the clavicle. Its greatest diameter may measure from 3 to 5 cm. The upper margin of the defect is usually irregular in outline and of slightly increased density. Under such conditions, the anomalous development of the depression appears as a large bony defect and may easily be mistaken for a destructive process.

Pendergrass and Hodes (1) state that the anomaly is usually bilateral and in their small series occurred only in muscular males. In the case recorded here the anomaly was unilateral in a young male of rather slight muscular development. The defect was discovered accidentally on a roentgenogram of the chest and the complete lack of any symptoms referable to the suspected region made it seem highly unlikely that it was due to a pathological process. Reference to the article of Pendergrass and Hodes confirmed the belief that the defect represented an anomalous development of a normal anatomical landmark. It is important that the possibility of such an anomaly be kept in mind.

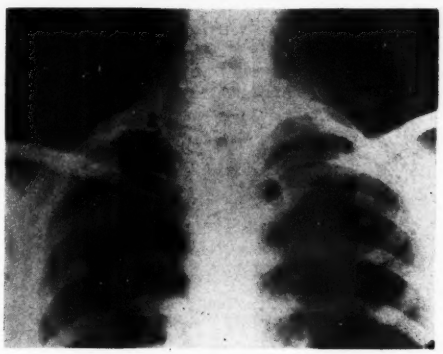


Fig. 1. Large bony defect in the right clavicle, representing the rhomboid depression, indicated by arrow no. 1. Arrow no. 2 points to the anomalous first and second ribs on the left side.

REPORT OF CASE

A male, seventeen years of age, not very muscular in development, was referred for roentgen study of the neck and chest in an effort to determine the nature of a hard mass located just above the inner end of the left clavicle. The patient was in good health and had no complaints of any kind. The mass, which was of bony hardness, had been dis-

[1] Accepted for publication in April 1940.

covered accidentally by the patient several weeks prior to examination.

A roentgenogram was made of the entire chest (Fig. 1) and it was found that the left first rib was rudimentary, its anterior end articulating with the mesial border of the second rib. The bony arch of the second rib was hypertrophied and it was this prominence which was palpated as a hard mass in the left supraclavicular area. During the study of the film, a large defect was noted on the inferior border of the inner end of the right clavicle. Because of the reasons stated previously it was felt that the defect represented an unusually well developed rhomboid depression.

SUMMARY

The rhomboid depression of the clavicle is described and illustrated.

It is important to differentiate such an anomaly from the various pathological processes which may involve the same region.

856 Central Ave., Far Rockaway, N. Y.

REFERENCE

1. PENDERGRASS, E. P., AND HODES, P. J.: Rhomboid Fossa of Clavicle. Am. J. Roentgenol. 38:152-155, July 1937.

CASE REPORTS

Gas Gangrene of the Uterus[1]

M. H. POPPEL, M.D., and M. SILVERMAN, M.D.[2]
New York, N. Y.

Gas gangrene of the uterus is a rare condition with a high mortality rate. The literature reveals about 175 cases diagnosed mainly at autopsy. Hill in 1936 reported a detailed study of 30 cases with a mortality of 63 per cent. In 4 cases the diagnosis was established antemortem by physical examination and laboratory methods; in 16 cases the diagnosis was not suspected until autopsy. About 75 per cent of the cases were associated with abortions.

The roentgen diagnosis of gas gangrene of the uterus is extremely rare. The literature yields but one example, reported by Russell and Roach in 1939. Unfortunately, these authors did not publish the film upon which they based their diagnosis. No illustration, therefore, depicting gas gangrene of the uterus could be found in the literature.

The rarity of films showing gas gangrene of the uterus is dependent not on any diagnostic difficulty from the roentgenologic standpoint but rather upon failure to recognize the advantage of x-rays as a diagnostic modality over the ordinary physical examination and laboratory methods. Since gas is one of the by-products of this type of infection and since it is formed early and easily detected roentgenographically, it follows logically that the roentgenogram is the ideal diagnostic agent.

Gas in the uterus may be of accidental or infectious origin; in the latter case it is caused by the entrance or introduction of gas-forming bacilli into the generative tract, where the presence of necrotic tissue provides favorable soil. As the infection spreads in the fulminating types, the involved tissue becomes gangrenous and full of gas bubbles.

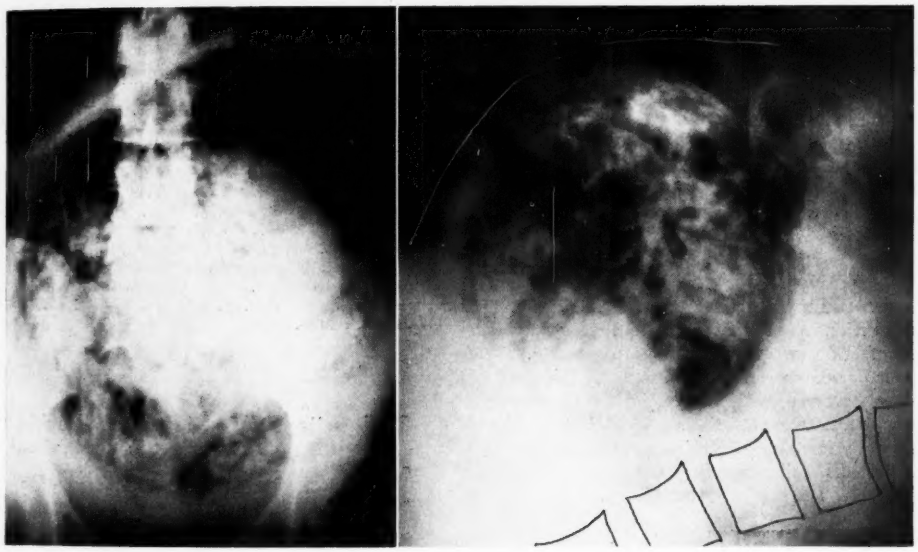


Fig. 1. Enlarged fibroid uterus showing numerous globules of gas due to gas gangrene. In the lateral view (right) the lumbar vertebrae and the anterior abdominal wall have been touched up.

There are various bacilli capable of gas formation in the tissues and it may be extremely difficult to differentiate between the types. Gas gangrene and gas in the tissues are not synonymous with *B. welchii* infection, only a small percentage of cases being due to that organism. Gas gangrene is a general term covering infections due to one or more gas-forming anaerobes of varying degrees of virulence. The varieties most to be feared are *B. welchii*, *B. oedematiens*, and *Vibrion septique*. *B. welchii* is a heavy, encapsulated, anaerobic, non-motile, non-liquefying bacillus which is gram-positive.

As pointed out above, roentgenography is the

[1] From the Division of Radiology of the Kings County Hospital of the Department of Hospitals of the City of New York, Dr. Richard A. Rendich, General Director. Accepted for publication in August 1940.

[2] Dr. Silverman now resident in Washington, D. C.

method of choice for the diagnosis of gas gangrene of the uterus. The gas bubbles are demonstrable in the roentgenogram and the extent of the involvement can be accurately determined, making early treatment possible. Guinea-pig inoculation with material from anaerobic lactose agar cultures and smears from the labia, vagina, and uterus is another diagnostic procedure. At operation gas escapes when the infected tissue is opened and the uterus appears black, friable, and extensively necrotic. From his series of cases, Hill concludes that the clinical detection of gas gangrene in the uterus is difficult and often impossible.

The following signs and symptoms suggest the diagnosis in a pregnant woman, especially in those with a history of abortion and manipulation: rapidly developing jaundice (toxic); increasing pulse rate; progressive excruciating uterine pain, otherwise unexplained; sudden collapse without obvious reason; gas in the vaginal secretions; crepitus over the uterus.

Treatment may be conservative (serum and transfusions), surgical (hysterectomy, serum, and transfusions), or by roentgen rays. A streptococcus peritonitis contraindicates surgery.

According to Kelly and others, roentgen therapy approaches a specific for gas gangrene anywhere in the body when used early and as outlined by its advocates. It is by far the most effective measure as yet employed. These writers recommend that roentgen therapy be given at the first suspicion of gas infection by *B. welchii* and in all cases in which the infection would be likely to develop. The technic depends upon the location and thickness of the part involved, with kilovoltage and filtration to insure adequate penetration. About 100 r per area twice daily for three to five days, depending on the progress of the disease, is the usual dose. The use of serum or surgery is not necessary.

CASE REPORT

A twenty-nine-year-old colored woman was admitted to the Kings County Hospital on Feb. 6, 1940, with a history of slight vaginal bleeding for the past three months. Her last menstrual period began on Oct. 15, 1939. On the day before admission she experienced cramps and increased vaginal bleeding. A few minutes prior to admission there occurred a spontaneous abortion. The placenta was not passed.

At the time of admission a large fibroid uterus extending up to the umbilicus was palpated. Small fragments of placental tissue were removed from the cervix.

On Feb. 9 the patient became acutely ill. Abdominal palpation was suggestive of crepitus. Roentgen examination of the abdomen revealed numerous globules of gas (emphysema) distributed throughout, and limited to, the enlarged uterus, indicative of gas gangrene.

A hysterectomy was done the same day and gas was seen to escape at operation. The uterus was black and extensively necrotic. Large doses of serum were administered daily until the patient died three days later.

Pathological Report: The uterus measured 12 × 15 × 30 cm., was purplish in color, and gangrenous. It contained a very large necrotic fibroid 13 cm. in diameter. The extreme necrosis had been caused by *B. welchii*, which was obtained by culture at the time of operation. Microscopically it was noted that in spite of the extreme necrosis there was little inflammatory reaction.

114 E. 54th St., New York, N. Y.

REFERENCES

HILL, A. M.: Post-abortal and Puerperal Gas Gangrene: Report of 30 Cases. Brit. J. Obst. & Gynec. **43:** 201–251, April 1936.

KELLY, J. F., DOWELL, D. A., RUSSUM, B. C., AND COLLIEN, F. E.: Practical and Experimental Aspects of the Roentgen Treatment of B. welchii (Gas Gangrene) and Other Gas-Forming Infections. Radiology **31:** 608–619, November 1938.

LASH, A. F.: Puerperal Sepsis: B. welchii Fatal Types. Am. J. Obst. & Gynec. **25:** 288–299, February 1933.

RUSSELL, P. B., JR., AND ROACH, M. J.: B. welchii Infections in Pregnancy, with Review of Literature and Report of 17 Cases. Am. J. Obst. & Gynec. **38:** 437–448, September 1939.

TOOMBS, P. W., AND MICHELSON, I. D.: Clostridium welchii Septicemia Complicating Prolonged Labor Due to Obstructing Myoma of Uterus, with Report of Case. Am. J. Obst. & Gynec. **15:** 379–389, March 1928.

Cholecystographic Diagnosis of Double Gallbladder with Pathologic Verification[1]

W. ROGER SCOTT, M.D., S. SANES, M.D., and HERBERT A. SMITH, M.D.

Niagara Falls, N. Y.

As far as we can determine, the following is the first complete report in the medical literature of a double gallbladder diagnosed by cholecystography and subsequently proved at operation and by pathologic examination.

History: A 57-year-old white man was admitted to the Niagara Falls Memorial Hospital, service of Dr. Fred Leighton, on May 12, 1940, with a complaint of distress induced by numerous foods. The past history included appendectomy, tonsillectomy, removal of a pharyngeal polyp with atypical epithelial proliferation, undulant fever, passage of renal gravel, and pollinosis. For several years the patient had been disturbed by cardiac arrhythmia. Electrocardiograms by Dr. Grant Guillemont previous to admission to the hospital had shown this

[1] From the Niagara Falls Memorial Hospital and the University of Buffalo Medical School. Accepted for publication in November 1940.

to be due to frequent premature contractions. There was no evidence of myocardial impairment, either clinically or electrocardiographically.

Cholecystographic Reports: April 12, 1938. On a "scout" film no calculi were noted in the gallbladder area. A series of films following oral administration of dye showed an excellent gallbladder shadow, in reasonably normal location (Fig. 1). The gallbladder had a somewhat doubled appearance in its mid-portion. Approximately halfway from its upper end down to its fundic pole were two somewhat rounded areas of decreased density, each fainter defect about 4 mm. in diameter. A third defect, slightly oval in shape, 6 mm. in diameter, was observed close to the lower pole. The two upper defects were suggestive of small papillomas; the defect at the fundic pole was considered to be an adenoma or non-opaque calculus.

Following the examination on April 18, 1940, a gallbladder dye series was made in the Cleveland Clinic. The roentgenograms of this series were reviewed at the Niagara Falls Memorial Hospital. The following comment is from a letter written on May 1 to the Cleveland Clinic: "In film marked

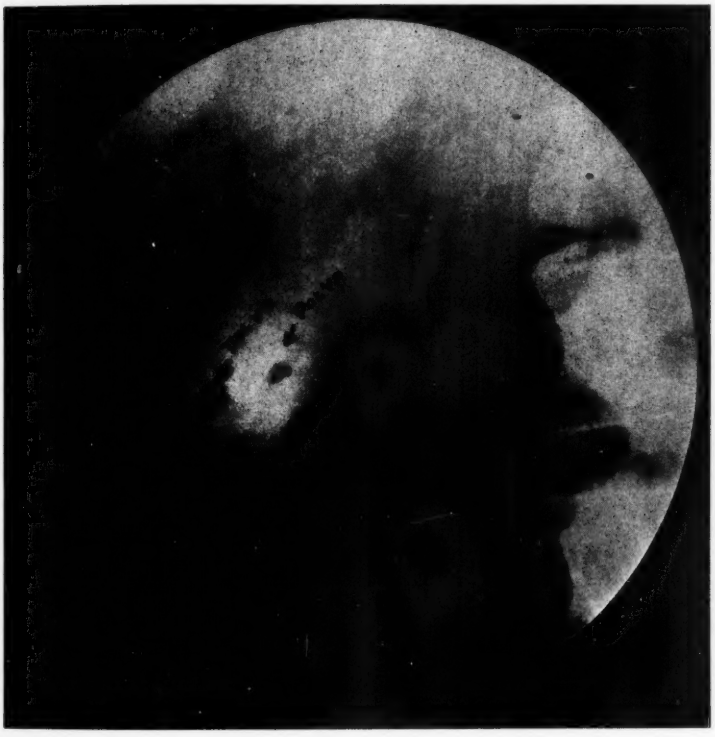


Fig. 1. Cholecystogram of double gallbladder April 12, 1938. Note double appearance, and two negative shadow areas interpreted at that time as papillomas.

less than 5 mm. in diameter, strongly suggesting papillomas. Following a fat meal the gallbladder showed good emptying power.

April 18, 1940. Again no calculi were noted on a "scout," film. Following oral administration of dye (double-dose method), the gallbladder shadow appeared fairly normal in size, and somewhat lobulated (Fig. 2). Concentration of the dye was good. Emptying after a fat meal was satisfactory. There was one defect in the gallbladder shadow, measuring 4 mm. in diameter, 3.1 cm. above the lower pole. Lateral to this defect, on a level with the transverse process of the second lumbar vertebra, was a much R 10, which shows some contraction of the gallbladder, the gallbladder shadow has a somewhat lobulated appearance, almost that of a double gallbladder with the uppermost small, rounded, punched-out, non-opaque area(s) in the 'neck' of this 'second gallbladder.'. . . admit the probability that the area of negative density in the lower pole of the galibladder may well be a calculus. Possibly the upper ones may also be calculi, but they are so sharply punched out that I raise the question of small soft-tissue tumors—papillomas. . . . ."

Laparotomy was performed May 13, 1940. The liver was found to be enlarged; the inferior margin

of the right lobe was sharp. The capsule above the gallbladder was fibrosed. The gallbladder was adherent to the stomach and duodenum. One stone the size a bean was felt. Upon cholecystectomy the specimen was recognized to be a double gallbladder.

Pathologic Description: The surgical specimen when received was partially opened, as shown in Figure 3. Inspection at once revealed that we were dealing with a double gallbladder and a double cystic duct. The two gallbladders and cystic ducts lay side by side, separated by connective tissue.

posits which ranged from pin-point size to 0.3 cm. in length. The largest cholesterol polyp was situated in the neck, being 0.6 cm. in length. The wall was 0.15 cm. thick.

The serosa of the double gallbladder showed evidences of fine adhesions on its free surface. There were no hemorrhages. One stone (0.8 × 0.7 cm.), oval in shape, of combination type, chiefly cholesterol, and one "papillomatous" cholesterol polyp, 0.65 × 0.4 × 0.25 cm., were received separately. On x-ray examination, the stone showed moderately

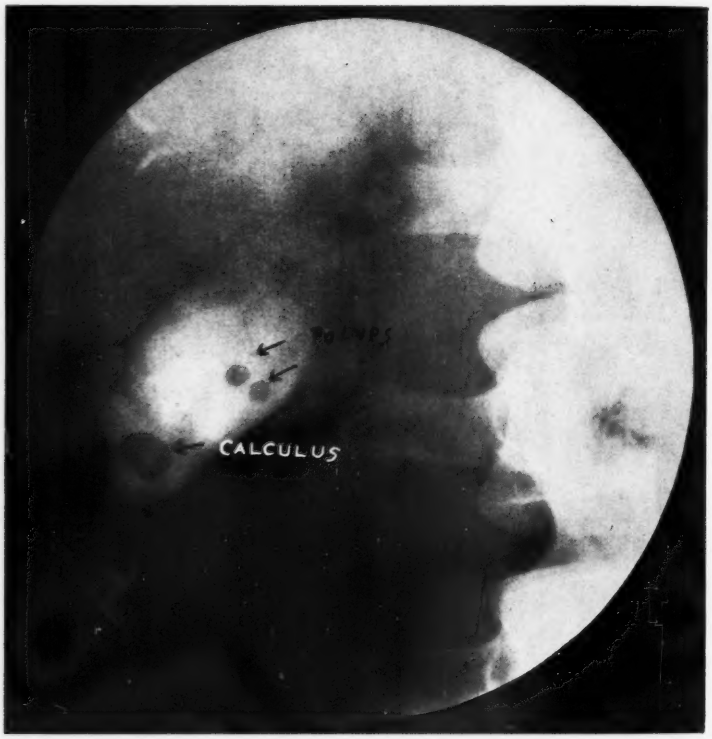


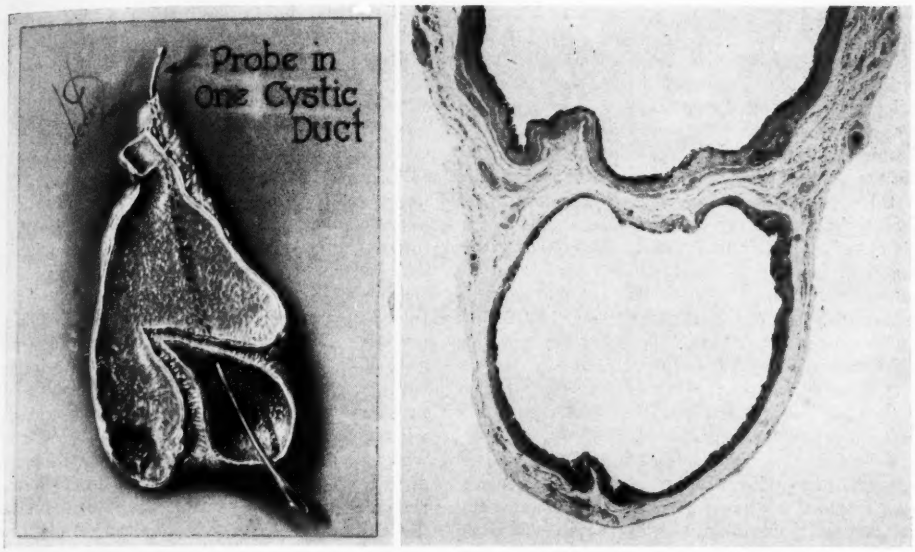
Fig. 2. Cholecystogram of double gallbladder April 18, 1940. Note double appearance and negative shadows demonstrated in Fig. 1; also shadow at lower pole caused by non-opaque stone, not previously demonstrated.

What corresponded to the gallbladder with a large area of negative density in the lower pole, measured 6 × 3.1 cm. The mucosa showed bile imbibition. There was fine cholesterolosis with a few minute, cholesterol, polypous deposits. In the fundus was a pressure mark from a stone, 1.3 × 0.8 cm. The wall was 0.2 cm. thick.

The other gallbladder, which in the films showed two small punched-out areas of negative density in its upper part, measured 3.6 cm. in circumference. The mucosa showed bile imbibition, and cholesterolosis was marked, with polypous cholesterol dense central areas. Each cystic duct measured 1.6 cm. in length × 0.6 cm. in circumference.

In both gallbladders the lining was fairly well preserved (Fig. 4). The tunica propria showed cholesterolosis and round-cell infiltration. These findings were most marked in the gallbladder without the gross pressure mark from stone. Glands penetrated to the muscularis and subserosa; the lumens of some contained desquamated epithelial cells. The muscularis of the gallbladder with a gross pressure mark from stone was moderately hypertrophic.

The two gallbladders were separated by the sub-



Figs. 3 and 4. Gross surgical specimen showing double gallbladder with two cystic ducts and (right) histologic section through mid-portion of double gallbladder. In the gross specimen note the pressure mark from stone in the fundus of the completely opened gallbladder. The polyps were in the second gallbladder, in which the probe is pictured.

serosa. Neither was completely invested by serosa. The subserosa disclosed moderate fibrous thickening and fat growth, and slight round-cell infiltration. Section through the largest attached cholesterol polyp in the neck area of the one gallbladder confirmed the gross diagnosis. The polyp had a "papillomatous" configuration. Both cystic ducts were involved by inflammatory changes similar to those in the gallbladder. There was no evidence of malignant growth.

Roentgenograms of the stone and of one of the polyps were made. The stone had low density at the periphery surrounding a somewhat more dense central portion. The latter was not densely solid but presented a somewhat striated appearance, not unlike a tiny snow crystal. The polyp showed slightly less density than did the periphery of the stone.

Pathologic Diagnosis: Double gallbladder and double cystic duct; slight chronic cholecystitis; cholelithiasis; cholesterolosis; cholesterol polyps.

Postoperative Course: Immediately following the operation the cardiac arrhythmia was markedly accentuated, the heart rate becoming very rapid. Two months after the operation, however, the premature contractions were much less frequent in occurrence, although the patient was still somewhat disturbed by them. Our cardiologist advises us that extrasystolic cardiac arrhythmias are a more or less frequent concomitant of gallbladder disease, although of course not diagnostic of such a condition, *per se*.

COMMENT

From a roentgenographic standpoint it is interesting to note that the polyps appeared to enlarge very little, if any, during a period of two years, their location remaining constant (Figs. 1 and 2). It seems reasonable to believe that a polyp may have been the basis of the oval stone which was found in the lower pole of one of the two gallbladders, and therefore to believe that if this patient had not come to operation when he did, multiple calculi might have developed.

Duplication of the gallbladder is a rare anomaly. Boyden (1) estimates its occurrence as 1 in 3,000 to 4,000. According to Bryan (2), fewer than 40 double gallbladders have been described in the modern literature. Walters and Snell (3) list 4 additional examples.

As a rule, duplication of the gallbladder is discovered first at operation or autopsy. In only 9 cases (2, 4–8) has the anomaly been detected by roentgen examination. Nichols (4) inferred a correct diagnosis from the evidence of 2 rows of opaque gallstones in his films. Climan (5), Hayes (6) (2 cases), Cave (7), Bryan(2), and apparently Weiss (8) (3 cases) visualized double gallbladders with dye. The first four writers, however, could not confirm their diagnoses anatomically because, in the absence of pathologic findings on x-ray examination other than the anomaly, and in the presence of symptomatic relief with medical therapy, their patients were not operated on. Weiss makes no specific

statement as to whether his x-ray reports were verified pathologically.

Our case thus becomes the first, completely recorded, in which a double gallbladder was visualized radiographically by dye and subsequently proved at operation and by pathologic examination. Also of unique interest from a radiographic standpoint was the visualization of the anomalous gallbladder on three occasions in two years by two different laboratories. Further, the double gallbladder in this case is the first in which cholesterol polyps—diagnosed from our x-ray films as "soft-tissue tumors—papillomas (?)"—were demonstrated in cholecystograms. Finally our case, while the fourth double gallbladder listed in the literature in which cholelithiasis was noted radiographically, represents the first in which the roentgenologist by repeated examinations disclosed the development of a practically non-opaque gallstone.

Of practical value is knowledge of the various types of duplication of the gallbladder. On embryologic and anatomic grounds these have been classified as (1) ductular, with two cavities and two cystic ducts, (2) bilobular, with two cavities and one cystic duct, (3) diverticular, with one large cavity communicating with one or more smaller cavities, and (4) trabecular. In a strict structural sense only the ductular form, which our specimen illustrates, can be considered a true double gallbladder.

NOTE: We are indebted to Mr. Melford D. Diedrick for illustrations.

621 Tenth St., Niagara Falls, N. Y.

BIBLIOGRAPHY

1. BOYDEN, E. A.: The Accessory Gall Bladder. Am. J. Anat. **38:** 177, 1926.
2. BRYAN, L.: Double Gall Bladder. Radiology **35:** 242, 1940.
3. WALTERS, W., AND SNELL, A. M.: Diseases of the Gallbladder and Bile Ducts. Philadelphia, W. B. Saunders Co., 1940, pp. 33–34.
4. NICHOLS, B. H.: Double Gall Bladder. Radiology **6:** 255–256, 1926.
5. CLIMAN, M. Duplication of the Gallbladder Demonstrated by Cholecystography. M. J. & Rec. **130:** 73–74, 1929.
6. HAYES, R.: Double Gall Bladder with Double Cystic Duct. Radiology **16:** 66–67, 1931.
7. CAVE, P.: Two Cases of Double Gallbladder. Lancet **1:** 751–752, 1931.
8. WEISS, S.: Diseases of the Liver, Gall Bladder, Ducts and Pancreas: Their Diagnosis and Treatment. New York, Paul B. Hoeber, Inc., 1935, pp. 102–112.

Chronic Sclerosing Non-Suppurative Osteomyelitis of Garré: Report of a Case with Involvement of the Cuboid Bone[1]

THOMAS HORWITZ, M.D.
Philadelphia, Pa.

A review of the literature indicates that the clinicopathologic picture of sclerosing non-suppurative osteomyelitis has been generally misunderstood. Not only has there been lack of unanimity in the proper interpretation of this osseous lesion, but there has been actual distortion of the features which Garré (1, 2) defined under this heading. Essentially, sclerosing osteomyelitis of Garré, according to the translation by Jaffe and Lichtenstein (3) of Garré's original article (1), in which he described the "sclerosing non-suppurative form" as one among a variety of expressions of acute osteomyelitis, includes ". . . . those infectious osteomyelitides which leave behind merely a distention and thickening of the bone, without leading to the development of suppuration and fistula formation. They set in in typical fashion quite acutely, at least in the majority of cases, and run their course with high fever, swelling of the extremity, painfulness and distention of the bones, and indeed even with considerable infiltration of the soft parts, which permits the expectation of prompt formation of abscesses. Instead, however, the infiltration regresses quite slowly, while the fever has already dropped and the patient is advancing slowly toward healing. Nothing remains but a more or less considerable distention of the bone."

Garré suggested that a sequestrum might act as a chronic irritant and thus stimulate bone formation without pus formation, and that this sequestrum could be taken care of by the body tissues without fistulization. Peters (4), however, in a later report from Garré's clinic, indicated that in some of these cases sequestra and fistulae developed months or years after the subsidence of all acute manifestations. This would suggest that some of the cases described in the pre-Roentgen era as instances of sclerosing non-suppurative osteomyelitis had been examples rather of osteomyelitis in which the acute manifestations had subsided without surgical interference, but which had progressed into a chronic stage, associated with the formation of sequestra and ultimately with fistulization.

This osseous lesion has become a rarity largely because more critical diagnostic criteria are excluding other types of osteomyelitis and are differentiating other localized sclerosing lesions of bone. It is also likely that the earlier application of medical and surgical measures in the treatment of acute osteomyelitis has diminished the frequency of transformation of the acute stage into the more chronic forms

The case here reported as an instance of sclerosing osteomyelitis of Garré presented the following features: (1) acute onset, at the age of thirteen, of painful, non-fluctuant swelling in the lateral portion of the right foot, associated with high fever, and without definite preceding trauma or related infection elsewhere in the body; (2) recurrent episodes, over a thirteen-year period, of fever and of localized pain, tenderness, and heat in this same region of the foot, occurring three to four times each year for approximately one week at a time, with

[1] Accepted for publication in February 1941.

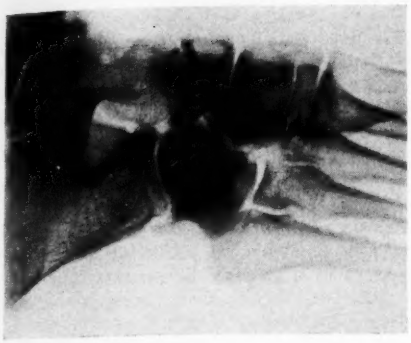


Fig. 1. Lateral-oblique roentgenogram of the right foot, showing the localized sclerosing lesion of the cuboid bone and the surrounding normal foot bones and their articulations.

totally asymptomatic intervals; (3) absence of gross suppuration and fistulization; (4) roentgenographic evidence of diffuse, irregular densification of the involved foot bone, the cuboid; (5) histologic evidence of local multiple abscesses in various stages of healing, of marrow scarring, of bone destruction without sequestrum formation, and of extensive local bone formation and bone deposition; (6) recovery following complete excision of the involved tarsal bone.

CASE REPORT

A 26-year-old Italian male was hospitalized on Dec. 26, 1939, because of a painful, non-fluctuant swelling of the right foot in the region of the cuboid bone. He gave a history of recurrent episodes of fever and of painful swelling in the region of the right foot, three or four times each year over a thirteen-year period, each attack lasting for approximately one week. The interval periods were completely asymptomatic. Slight swelling had been present constantly in the region of the right cuboid bone, and became aggravated during the painful episodes. The onset of the first attack, at the age of thirteen, had been acute, associated with high fever. There had been no definite preceding trauma, and no antecedent or intercurrent infection elsewhere in the body. The swollen soft tissues, during this initial attack, had been incised, but no pus had been found and the wound had healed immediately thereafter. At no time during the thirteen-year period had there been evidence of suppuration or fistula formation. The last attack, during which the patient was admitted for surgical intervention, had been more severe and of longer duration (one month) than any of the previous episodes.

The outer aspect of the right foot, in the region of the cuboid bone, was swollen and exquisitely tender. There was local heat but no redness or fluctuation.

The blood picture was normal. The blood Wassermann and Kahn reactions were negative.

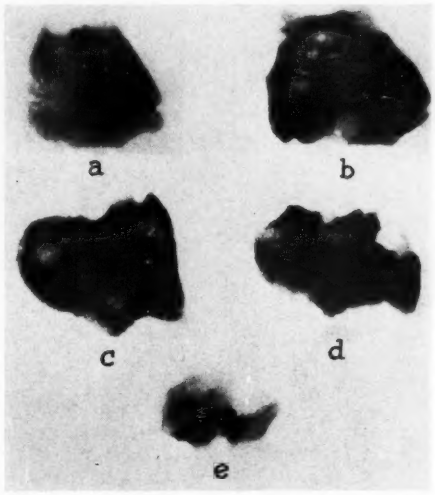


Fig. 2. Roentgenograms of five sagittal slivers of the excised right cuboid bone, arranged serially from (*a*) the most medial section (cuneiform surface) to (*e*) the most lateral section. The numerous and variable sized radiolucent areas represent localized multiple abscesses. Some of the large defects extend through the entire thickness of the tarsal bone. The bone is densified even in these thin slivers and the osteosclerosis is exaggerated about the larger radiolucent foci. The articulating and non-articulating surfaces show considerable irregularity.

The intracutaneous tuberculin test was negative. Repeated urinalyses yielded normal findings.

Roentgenograms of the right foot taken in 1938 and one year later, in November 1939 (Fig. 1), were identical. They revealed a mottled sclerosis of the entire cuboid bone, which was abnormally large. The other foot bones and their articulations appeared normal.

At operation the entire right cuboid bone was excised through a dorsolateral incision. No frank pus or sinus formation was encountered. The surrounding soft tissues appeared normal and the related articulating surfaces of the adjacent foot bones were intact. A primary closure of the wound was performed, the defect created by the removal of the cuboid bone being filled with a portion of the extensor digitorum brevis muscle.

Smears taken from the wound were negative, and aerobic and anaerobic cultures proved to be sterile. Healing occurred by primary intention. There was immediate relief of all symptoms, postoperatively, and there have been no recurrences during the subsequent period of one year. Although no attempt was made to reconstruct the defect created by removing the foot bone, the foot is stable and the functional result is excellent.

Histopathologic Features: The cuboid bone was enlarged (5 × 3.5 × 3 cm.) and much heavier

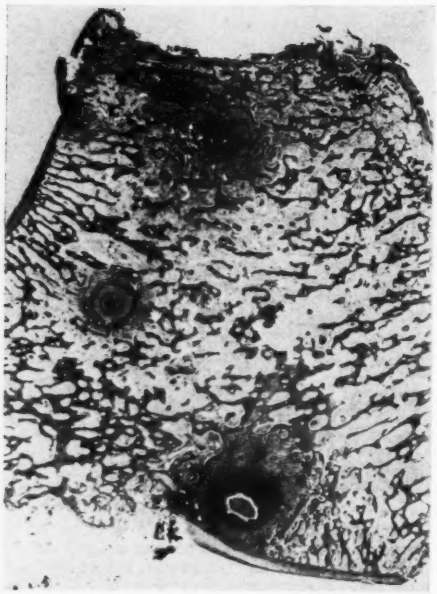


Fig. 3. Low-power photomicrograph (× *c.* 4) of a histologic section of the sliver illustrated roentgenographically in Fig. 2*b*. There are three large and two small abscesses demonstrating various stages of healing. The bone trabeculae throughout the section are thickened and the marrow spaces show marked scarring, these reactions being most prominent in the periphery of the abscess formations. The articular cartilage, especially that overlying the subchondral abscess, is considerably modified. (The complete break in the articular cartilage in the left upper angle is an artefact.)

than normal. Its articular cartilage was thinned and discolored, and appeared frayed in some places. The non-articulating surfaces were irregular, partly because of the formation of marginal exostoses. The bone was sectioned sagittally in five slivers. These sectioned surfaces showed the bone to be very sclerotic and several of them presented small, circular areas, some of which were solid while others contained semi-fluid material. No frank pus was encountered.

Roentgenograms of these bone slivers (Fig. 2) revealed features which the roentgenograms of the entire cuboid (Fig. 1) had failed to disclose clearly. The bone, which was densified even in these thin sections, was sprinkled with numerous circular and oval radiolucent areas of variable size. Some of the larger defects were traceable almost through the entire thickness of the tarsal bone. The osteosclerosis was exaggerated about many of these radiolucent foci. The non-articulating surfaces were very irregular, mainly in consequence of marginal bony proliferation, while the articulating surfaces showed considerable irregularity and thinning of the overlying cartilage.

The slivers were decalcified, embedded in celloidin, and stained with hematoxylin and eosin. Sections representing different levels in the sagittal plane demonstrated the following histologic features:

The spongiosa and peripheral cortex were dotted by numerous abscesses (of various sizes) consisting of collections of inflammatory cells (small and large lymphocytes, polymorphonuclear leukocytes, plasma cells), and varying amounts of connective tissue. The structure of these abscesses varied from those foci with a predominance of closely packed inflammatory elements, through different stages of healing, as manifested by increased amounts of compact, vascular connective tissue and smaller numbers of inflammatory cells, to complete healing, as represented by widespread fibrosis with poorly cellular hyalinizing connective tissue and few or no inflammatory cells (Fig. 3).

The bone trabeculae throughout the spongiosa and cortex were thickened by the deposit of well formed lamellar bone, lined by one or more layers of osteoblasts. The medullary spaces were correspondingly encroached upon, and showed increased marrow fibrosis with a sprinkling of focal collections of inflammatory cells (Fig. 3). Bony proliferation was most active in the periphery of the abscesses and in the adjacent bone trabeculae, especially in those regions manifesting early stages of healing. In these instances, islands of new bone formation were distributed throughout the more cellular connective tissue, while osteoid tissue and immature bone were deposited upon the adjacent trabeculae, often being delimited from the more mature bone by a dense cement line. In the periphery of these abscesses there was also evidence of active resorption of mature bone, a resorption usually vascular and only occasionally occurring through osteoclastic activity. Only here and there was a spicule of dead lamellar bone evident, in the interior of some of the abscesses.

The hyaline cartilage of the articular surfaces was irregular, fibrillated in some areas, and narrowed or even absent in other regions, so that the subchondral bone was exposed. It was found most extensively modified over subchondral abscess formations (Fig. 3).

DISCUSSION

The clinical, roentgenographic, and histologic features of the osseous lesion in this case serve to exclude such lesions as tuberculous and syphilitic osteitis, aseptic necrosis of bone, and benign or malignant neoplasia. Moreover, the acute onset with fever, the recurrent episodes of localized pain and swelling over a thirteen-year period without gross suppuration or fistulization, the roentgenographic features of a sclerosing bone lesion without sequestrum formation, and the histologic evidence of multiple bone abscesses in various stages of healing and limited to the confines of one bone, resemble accurately the features of the sclerosing non-sup-

purative subgroup of osteomyelitis as originally defined by Garré.

Jaffe and Lichtenstein (3) have indicated that some of the cases reported in the past as instances of sclerosing non-suppurative osteomyelitis of Garré, were probably instances of a benign osseous lesion, "osteoid-osteoma," developing in the shaft cortex of long bones. In fact, the former had been the preoperative diagnosis in several of their cases of cortical "osteoid-osteoma." This latter lesion, which Jaffe (5) reported previously in spongy bone, is composed of osteoid and calcified immature bone, arising from osteogenic connective tissue, while the surrounding spongy or cortical bone tends to undergo thickening. Attention to the perifocal sclerosis, especially where it dominates the roentgenographic picture and perhaps masks the "osteoid-osteoma" lesion proper, may lead to its interpretation as sclerosing osteomyelitis or chronic bone abscess. Although "osteoid-osteoma" has been reported by other authors under a variety of titles as a type of chronic bone infection, the evidence presented by Jaffe and Lichtenstein indicates that such an interpretation is unfounded and that the lesion is more properly considered a benign tumor of bone.

CONCLUSIONS

The clinical and laboratory features in a case presenting a sclerosing lesion of the right cuboid bone are interpreted as consistent with a diagnosis of sclerosing osteomyelitis of Garré. A survey of the literature indicates that the lesion originally described by Garré has been generally misunderstood, that few of the previously reported cases can be accepted as unequivocal instances of this condition, and that the clinical expression of this osseous lesion is now relatively uncommon.

32 So. 20th St., Philadelphia, Pa.

REFERENCES

1. GARRÉ, C.: Einige seltene Erscheinungsformen der akuten infectiösen Osteomyelitis. Festschrift zum Funfundzwanzigjähren Doktor- und Dozente Zubiläum von T. Kocher, Wiesbaden, 1891.

2. GARRÉ, C.: Ueber besondere Formen und Folgezustände der akuten infectiösen Osteomyelitis. Beitr. z. klin. Chir. **10:** 241–298, 1893.

3. JAFFE, H. L., AND LICHTENSTEIN, L.: Osteoid-Osteoma. Further Experience with This Benign Tumor of Bone, with Special Reference to Cases Showing the Lesion in Relation to Shaft Cortices and Commonly Misclassified as Instances of Sclerosing Non-Suppurative Osteomyelitis or Cortical-Bone Abscess. J. Bone & Joint Surg. **22:** 645–682, 1940.

4. PETERS, W.: Die seltenen Formen der Osteomyelitis. Beitr. z. klin. Chir. **117:** 186–199, 1919.

5. JAFFE, H. L.: "Osteoid-Osteoma," a Benign Osteoblastic Tumor Composed of Osteoid and Atypical Bone. Arch. Surg. **31:** 709–728, 1935.

EDITORIAL

Howard P. Doub, M.D., Editor

John D. Camp, M.D., Associate Editor

Radiological Society of North America: Annual Meeting, 1941
An Invitation from the President

As President of the Radiological Society of North America, it becomes my privilege in behalf of the Society and the Pacific Roentgen Society to extend to all radiologists and to all members of the medical profession a most cordial invitation to attend the Twenty-seventh Annual Meeting, in December. For the first time in many years a national radiological society is holding its annual meeting on the Pacific Coast, and for the first time in these many years the radiologists of the East and of the Middle West will have an opportunity to display the same loyalty in attending the meeting that has in the past been so willingly demonstrated by the Pacific Coast radiologists. San Francisco is a wonderful convention city and offers much of interest for everyone who attends this meeting.

The Scientific Program promises to be especially stimulating. There has been a wholesome response from both the radiologists and the medical profession in offering formal papers and in showing a willingness to take part in panel discussions on clinical radiology. The program is designed with the objective that every radiologist shall be able to take home something worth while to use in his daily practice.

The arrangements for the Refresher Courses have been completed by Doctor Ira Lockwood. To those attending the meeting these courses offer an unusual opportunity for study. The Scientific Exhibits are being arranged by Doctor Eldwin R. Witwer. These, together with the Commercial Exhibits will, as always, be an important part of the meeting.

The meeting will be held from December 1 to 5, 1941, with the Refresher Courses beginning on Sunday, November 30th, and reservations should be made promptly. The Hotel Fairmont will be the headquarters of the Society and the host to its members. The San Francisco radiologists and their wives will welcome you and your wives to San Francisco with the real California spirit. Come early to enjoy the big California-Stanford game and stay late to see the Pacific Coast.

W. WALTER WASSON, M.D.
President

An Invitation from the Local Committee

Historical in the highest sense must be the year 1941. Revolutionary changes in international affairs are, if anything, being exceeded by revolutionary changes in national affairs. Change is ever interesting, often stimulating, and occasionally progressive. The Annual Meeting of the Radiological Society of North America is ever progressive, often stimulating, and always new. And this year's meeting will be in keeping with the times—only more so!

Plan to come to San Francisco at the end of November. Read the preliminary program on the following pages. Consider the opportunity of seeing parts of this country which you may never have seen before, which this meeting gives you the chance to visit.

The Local Committees are striving diligently to make the program, both scientific and otherwise, as entertaining as possible. The Ladies Entertainment Committee has already completed plans for

a sparkling week. San Francisco is an excellent convention center. So make your plans now. Brush off the burro, dust off the serape, and start for the Pacific Coast—to steep yourselves in the legend that is California, and fold your year in the triple enjoyment of an Annual Radiological Society Meeting—in San Francisco.

Three major airlanes follow diverse routes to the city. From Chicago the TWA flies to Kansas City, south to Wichita, Amarillo, Albuquerque, over the Grand Canyon, Boulder Dam, and into Oakland.

The American Airlines reach Chicago from numerous eastern points. Thence they pass over St. Louis and Oklahoma City to Dallas. Leaving Texas, they follow the southern route to El Paso, Tucson, and into Los Angeles—a two-hour hop from San Francisco.

The most direct route between Chicago and San Francisco is that of the United Air Lines *via* Omaha, Cheyenne, or Denver, and Salt Lake City.

Motorists have a choice of four principal routes with a variety of interesting side trips on every highway.

The Old Spanish Trail or southern route leads from New Orleans or Dallas through the farm lands of Texas to historic San Antonio, winding into Tucson and Phoenix, through the fertile Imperial Valley, into Los Angeles and San Francisco. The world-famed Carlsbad Caverns, in New Mexico, and Palm Springs, in California, can be visited on short side trips.

The Broadway of America starts at St. Louis, traverses the Oklahoma oil fields, touching Tulsa and Oklahoma City, passes through the Panhandle of Texas to Sante Fe and thence to the Painted Desert, Grand Canyon, Boulder Dam, the petrified forests of Arizona, and San Francisco.

The Lincoln Highway is the express route from the eastern seaboard to the west coast. From Chicago it stretches straight through the rich agricultural lands of Iowa and Nebraska into the rolling plains of Wyoming, and on to the Great Salt Desert in Utah. From Salt Lake City the highway crosses the Nevada desert into Reno, passes over the High Sierras and the California gold country to San Francisco.

The Shasta Route follows a more northern course across the western United States and down the coastline through Washington and Oregon to California. Through the Black Hills of South Dakota, touching at the Rushmore Memorial, traversing the storied Bad Lands to Yellowstone National Park, this highway leads either to Salt Lake and thence to California or across to Seattle, Glacier National Park, the Grand Coulee, and the redwood country bordering the Pacific to San Francisco.

High-speed bus accommodations are available on any of the motor routes and special train accommodations have been arranged by the Transportation Committee (see August RADIOLOGY, page xii), with and without stopovers for sightseeing.

THE LOCAL COMMITTEE ON ARRANGEMENTS

Hotel Fairmont, Headquarters for the Annual Meeting

Announcements

RADIOLOGICAL SOCIETY OF NORTH AMERICA: ANNUAL MEETING

PRELIMINARY PROGRAM

The Twenty-seventh Annual Meeting of the Radiological Society of North America will be called to order by the President, W. Walter Wasson, M.D., at 10:15 A.M., Monday, Dec. 1, 1941, in the Hotel Fairmont, San Francisco, California.

Dr. Wasson's summons to the meeting and the glowing invitation of the Local Committee on Arrangements appear elsewhere in this issue. Full details of the Refresher Courses were published in RADIOLOGY for September.

While the final program of the Scientific Sessions awaits completion, the preliminary outline indicates the excellence of the arrangement and the high quality of the papers.

There will be symposia on Brain Tumors, Fungus Infections, Cancer of the Breast, Inflammations, Gastro-intestinal Tract, Cyclotron, Lesser Circulation, Diseases of the Retroperitoneum, Leukemias and Lymphoblastomas, and Diseases of the Bones.

Among the papers to be presented are:

"The Pathology of Brain Tumors and Its Relation to Roentgenologic Diagnosis." EDWIN B. BOLDREY, M.D.

"The Reliability of Brain Tumor Localization by Roentgen Methods." FRED J. HODGES, M.D., and V. C. JOHNSON, M.D.

"Intracranial Calcifications of Non-neoplastic Origin." JOHN D. CAMP, M.D.

SAN FRANCISCO'S SKY LINE LOOKING EAST

In the background is a glimpse of the great San Francisco-Oakland Bay Bridge, which arches gracefully across the bay to join the sister cities of Berkeley, Oakland, and Alameda, to San Francisco.

"Application of Some New Technics in the Study of Brain Tumors." E. R. WITWER, M.D.

"Mucosography of the Organs of the Respiratory Tract." PEDRO L. FARINAS, M.D.

"Lung Tumors." FRANK S. DOLLEY, M.D.

"The Parallelism between Tuberculosis and Coccidioides." CHARLES E. SMITH, M.D.

"Acute Pulmonary Coccidioidomycosis—Roentgen Studies in an Epidemic." ROBERT A. POWERS, M.D.

"The Roentgen Diagnosis of Fungus Infections of the Lungs, with Special Reference to Coccidioides." RAY CARTER, M.D.

"The Roentgen Diagnosis of Fungus Infections of the Intestinal Tract." ALBERT K. MERCHANT, M.D.

FISHERMAN'S WHARF, SAN FRANCISCO
A miniature Italian harbor, gay with color and activity

"The Roentgen Diagnosis of Coccidioidal Infections of Bone." CARL BENNINGHOVEN, M.D., and EARL MILLER, M.D.

"General Management of Patients Undergoing Treatment for Malignancy." LOWELL GOIN, M.D.

"Roentgen Therapy in Cancer of the Breast: An Analysis of Our Experience at the State of Wisconsin General Hospital During the Last 12 Years." ERNST A. POHLE, M.D.

"The Place of Irradiation in Cancer of the Breast." FREDERICK O'BRIEN, M.D.

"Pathology of Breast Tumors." JOHN W. BUDD, M.D.

"Preoperative Radiation of Breast Tumors." ALBERT SOILAND, M.D.

"The Surgical Aspect of Carcinoma of the Breast." ALSON KILGORE, M.D.

"Radiation Osteitis of the Ribs." LESTER W. PAUL, M.D.

"The Mechanism of the Result of Roentgen Therapy." ARTHUR DESJARDINS, M.D.

"The Value of Roentgen Therapy in the Treatment of Pneumonia Which Fails to Respond to Sulfonamide Therapy." J. P. ROUSSEAU, M.D.

"The Roentgen Therapy of Sinus Disease." W. C. POPP, M.D.

"Further Observations on the Radium Treatment of Acute Postoperative Parotitis." ROBERT FRICKE, M.D., and GORDON F. MADDING, M.D.

"Roentgen Therapy of Peritonitis." JAMES F. KELLY, M.D.

"Roentgen Therapy of Postoperative Parotitis." EUGENE P. PENDERGRASS, M.D., and PHILIP J. HODES, M.D.

"The Dosage of X-radiation Incident to Fluoroscopic Examination." LOOMIS BELL, M.D.

"The Stomach and Small Intestines in the Infant." JOHN S. BOUSLOG, M.D.

"The Colon in the Healthy Newborn Infant." SAMUEL G. HENDERSON, M.D., and W. W. BRYANT, JR., M.D.

"The Clinico-Anatomical Aspect of the Lumbosacral Region." JOHN B. DE C. M. SAUNDERS, M.D., and VERNE T. INMAN, M.D.

"Thorotrast and the Diagnosis of Lesions Involving the Lower Spinal Canal." BERNARD H. NICHOLS, M.D.

"The Cyclotron and Nuclear Physics." PAUL C. AEBERSOLD, PH.D.

"Artificial Radioactive Elements in Metabolic Studies." JOSEPH G. HAMILTON, M.D.

"Artificial Radioactive Elements in the Treatment of Disease." JOHN H. LAWRENCE, M.D.

"Neutrons in the Treatment of Disease." JOHN C. LARKIN, M.D., and ROBERT S. STONE, M.D.

"Further Experiences in the Treatment of Lymphosarcoma with Radioactive Phosphorus." JOHN M. KENNEY, M.D.

"Emphysema in Cases of Angina Pectoris." WILLIAM KERR, M.D.

"The Studies of the Pulmonary Circulation by Means of Body Sectional Radiography." WENDELL SCOTT, M.D.

"The Value of Roentgen Ray in the Diagnosis of Endocrine Diseases." PAUL J. CONNOR, M.D.

"The Treatment of Endocrine Disorders by Small Doses of X-ray." JAMES H. HUTTON, M.D.

"The Roentgen Diagnosis of Vitamin Deficiency Cardiac Conditions." L. HENRY GARLAND, M.D.

"The Incidence of Multiple Primary Tumors and the Problems of Acquired Cancer Immunity." ERNST A. SCHMIDT, M.D.

"Technic and Results in Dental X-ray." GORDON FITZGERALD, D.D.S.

"The Specialist as a Medical Naval Officer." CAPTAIN A. H. DEARING, M.D.

"Micro-Film in Roentgenological Education." CHARLES G. SUTHERLAND, M.D.

"Fluorographic Examination of the Chest as a Routine Hospital Procedure." FRED J. HODGES, M.D.

"Endothelioma of the Pleura. Clinical and Roentgenologic Studies of Three Cases." HOWARD P. DOUB, M.D., and HORACE C. JONES, M.D.

"Carcinoma of the Lung in Infancy." HARRY HAUSER, M.D.

"Bone Lesions in Hodgkin's Disease and Lymphosarcoma." H. L. FRIEDELL, M.D.

"Influence of the Medium on the Radiosensitivity of Sperm." G. FAILLA, Sc.D.

"X-rays in the Management of Non-Malignant Diseases in the Organs of the Female Pelvis." BENJAMIN ORNDOFF, M.D.

"Treatment of Hemangiomata with Special Reference to Unsatisfactory Methods." WILBUR BAILEY, M.D.

"Observations on Radiodermatitis." ERICH UHLMANN, M.D.

"The Present Status of Roentgen Therapy in Chronic Paranasal Sinusitis." FRANK E. BUTLER, M.D., and IVAN M. WOOLLEY, M.D.

"Preliminary Report of the Effect of Combined Fever and Deep X-ray Therapy in the Treatment of Far Advanced Malignant Cases." H. S. SHOULDERS, M.D.

"The X-ray Treatment of Hyperthyroidism." ROBERT S. STONE, M.D., and MAYO H. SOLEY, M.D.

"Classification of Bone Tumors and Their Differential Features." KENNETH DAVIS, M.D.

"Clinical Pathology of Bone Tumors and Treatment." J. VERNON LUCK, M.D.

"The Development of Bone in Relation to the Formation of Neoplasms." KEENE O. HALDEMAN, M.D.

"Practical Considerations Regarding the Employment of Various Qualities of Roentgen Rays in Therapy." EDITH QUIMBY, Sc.D.

"Radiation in Corpus Uteri Cancer." IRA I. KAPLAN, M.D.

The Carman Lecture will be delivered on Dec. 2 by Dr. W. EDWARD CHAMBERLAIN of Philadelphia, who will speak on "Fluoroscopes and Fluoroscopy."

TRANSPORTATION TO SAN FRANCISCO

The Transportation Committee advises all those who may be going to San Francisco by train, or who even think they may go by train, to fill in and mail the blank on page xii of the August issue of RADIOLOGY. Unless sufficient response is secured from those who may be going, it will be impossible to make arrangements with the railroads for special equipment.

W. R. SCOTT, M.D.
Niagara Falls, N. Y.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY

At the recent Radiological Conference held in Denver, Colo., under the auspices of the Denver Radiological Club there was formed the Rocky Mountain Radiological Society with 42 charter members. Dr. Leonard G. Crosby of Denver was elected president and Dr. Alfred M. Popma, Boise, Idaho, secretary. The next annual meeting will be held in Denver during the summer of 1942.

NORTH DAKOTA RADIOLOGICAL SOCIETY

Radiologists of North Dakota have recently organized the North Dakota Radiological Society. L. A. Nash, M.D., St. John's Hospital, Fargo, was elected secretary. Meetings are to be held by announcement.

BROOKLYN ROENTGEN RAY SOCIETY

The newly elected officers of the Brooklyn (N. Y.) Roentgen Ray Society are: President, Dr. George Cramp; Vice-President, Dr. Louis J. Taormina; and Secretary-Treasurer, Dr. Leo Harrington.

In Memoriam

WM. CLARK WESCOTT, M.D.

Dr. Wm. Clark Wescott died on July 26, 1941, at the age of seventy-three in Atlantic City, N. J. Dr. Wescott was born in Atlantic City in 1868, and his professional life was spent there. He was a graduate of the Philadelphia College of Pharmacy and it was as a pharmacist that he first became interested in roentgenology. In 1908 he was graduated from the University of Pennsylvania Medical School and he subsequently studied in Vienna, Stockholm, and Paris. He was head of the Department of Radiology at City Hospital, Atlantic City, and a member of various medical and radiological organizations both in America and abroad. He was a former vice president of the Radiological Society of North America and a fellow of the American College of Radiology.

Books Received

Books received are acknowledged under this heading, and such notice may be regarded as recognition of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

DISEASES OF THE NAILS. Second Edition. By V. PARDO-CASTELLO, M.D., Assistant Professor of Dermatology and Syphilology, University of Habana. With a Foreword by Howard Fox, M.D., Professor of Dermatology and Syphilology, New York University, Bellevue Hospital Medical College. A volume of 193 pages with 94 illustrations. Published by Charles C. Thomas, Springfield, Illinois, 1941. Price $3.50.

STANDARD RADIOGRAPHIC POSITIONS. By NANCY DAVIES, M.S.R., Senior Radiographer, Royal Surrey County Hospital, Guildford; Late Senior Radiographer, Caernarvonshire and Anglesey Infirmary, Bangor, N. Wales; Late Senior Radiographer, Royal Infirmary, Worcester, and URSEL ISENBURG, M.S.R., Radiographer to the Charterhouse Rheumatism Clinic, London; Research Worker, Institut Municipal d'Electro-Radiologie (Prof. Zimmern), Paris, 1933–35; Radiographer, Rudolf Virchow Hospital (Dr. G. Bucky), Berlin, 1929–33. A volume of 136 pages with 103 illustrations. Published by The Williams & Wilkins Company, Baltimore, 1941. Price $2.00.

DAS SCHICHTBILD DER LUNGE, DES TRACHEOBRONCHIALBAUMS UND DES KEHLKOPFES (The Tomographic Picture of the Lungs, the Tracheobronchial Tree and the Larynx), by KURT GREINEDER, Dozent in Roentgenology at the University of Berlin, Chief of the University Roentgen Clinic at Robert Koch Hospital. A volume of 250 pages with 509 illustrations. Published by Georg Thieme, Leipzig, 1941. Price 37.30 R.M. bound.

Book Reviews

AN INTRODUCTION TO GASTRO-ENTEROLOGY. By WALTER C. ALVAREZ, M.D., The Mayo Clinic, Rochester, Minnesota. A volume of 778 pages with 186 illustrations. Published by Paul B. Hoeber, Inc., New York City, 1939. Price $10.00.

No one can read Doctor Alvarez's book, "An Introduction to Gastro-Enterology," without being impressed by his careful review and evaluation of earlier contributions, both clinical and experimental, relevant to this subject. The enormous amount of material compiled is supplemented by his vast personal experience. Doctor Alvarez states in his preface that research workers and students need to know where the big gaps in our knowledge occur—gaps that should be filled. He has met this need most adequately.

The present work, though it is designated as the Third Edition of The Mechanics of the Digestive Tract, is almost completely new. Not only is it indispensable to the research worker, but it is both fascinating and instructive for the surgeon and practitioner, who will find here a scholarly consideration of most of their problems, whether solved or unsolved.

The chapter on books and reading is a most valuable one to all students and workers interested in gastro-enterology.

One cannot appreciate the fascination of this great fund of up-to-date information until he has read the book.

X-RAY THERAPY OF CHRONIC ARTHRITIS (Including the X-ray Diagnosis of the Disease). By KARL GOLDHAMMER, M.D., Associate Roentgenologist, St. Mary's Hospital and Quincy X-ray and Radium Laboratories; formerly Roentgenologist, University of Vienna. Foreword by Harold Swanberg, M.D., Editor Mississippi Valley Medical Journal and the Radiologic Review; Roentgenologist St. Mary's Hospital and Blessing Hospital; Director Quincy X-ray and Radium Laboratories. A volume of 131 pages with twenty-four illustrations, two roentgenograms and four tables. Published by the Radiologic Review Publishing Company, Quincy, Illinois, 1941. Price $2.00.

The author, formerly chief of the Roentgen Laboratory of the First Anatomical Institute of the University of Vienna but now residing in Quincy, Illinois, herein presents a "preliminary report" based chiefly on 100 patients treated in Quincy but also on a "wide experience gained in Vienna on hundreds of patients during fifteen years of practice." Ten chapters comprise this small volume. In Chapter 1 the clinical and pathologic aspects of chronic arthritis are chiefly considered. In Chapter 2, which comprises forty-one pages, or a third of the volume, the roentgenologic findings in chronic arthritis are discussed. But since "it is difficult to find appropriate roentgenograms showing the features necessary for proper explanation of these very variable diseases," the author decided to illustrate the discussion, not by reproductions of roentgenograms, but by twenty-four drawings made from several roentgenograms representing different stages of each of several diseases. "In this manner," he states, "the most striking and essential roentgenologic features are conspicuously pointed out." The reviewer agrees that explanatory drawings of roentgenograms are helpful to the average physician none too familiar with the roentgenologic aspects of joints, but the inclusion of not a single roentgenogram in this chapter would seem to be an unfortunate

omission. A selection of representative roentgenograms *and* explanatory diagrams would have been more helpful to the average reader. The diagrams are for the most part satisfactory and instructive, but the author discloses some lack of clinical experience (in contrast to his roentgenologic knowledge) when he shows hypertrophic arthritis involving the metacarpophalangeal joints of the hand and atrophic arthritis affecting the terminal phalangeal joints. The assumption that these involvements commonly occur is contrary to clinical experience. In this respect and in others the book could have been materially improved had it been submitted to a physician with a wide *clinical* experience with the arthritides.

Chapter 3, a brief discussion of the roentgenologic differential diagnosis, is not particularly helpful. This chapter contains no diagrams or roentgenograms and in it the author discusses rather cursorily types of arthritis not previously illustrated, among them some contentious forms (such as menopausal arthritis) not accepted as entities by critical rheumatologists.

Chapter 4 is entitled the "History of X-ray Therapy of Chronic Arthritis" but does not bear out its formidable title. It is sketchy; indeed, only two early European references and two early American references are specifically mentioned; all other work is dismissed and the chapter concludes with a group of uncritical questions from about a dozen recent sources, most of which have appeared since 1933. On page 75 the author claims to have made a "critical review" of all these papers, yet in the material described treatment of such vague conditions as "polyarticular pains," "acute arthritis," "chronic arthritis," "chronic rheumatism," is referred to, in most instances with no qualifying etiologic term whatever.

In Chapter 5, "How Do X-rays Act in Chronic Arthritis?," the author concludes (without proof) that roentgen rays help the arthritic patient by producing "actively hyperemic stimuli;" that is, because of capillary vasodilation, "cessation of the nutritional disturbances in the diseased joint may be assumed." This explanation presumably applies to infective arthritis also, because, although "x-rays do not affect the bacteria themselves, they change the tissue in such a way that the microorganisms meet with a less favorable media for their growth" (Chapter 6).

So certain of the value of roentgen therapy is the author that he recommends (page 89) prophylactic roentgen ray treatment in cases in which roentgenograms made for other reasons reveal "an arthritis [type undesignated] without the patient having any clinical symptoms." Were roentgen therapists in a position to treat all patients suffering from symptomless hypertrophic arthritis, which is almost universally present among persons more than fifty years of age, they would indeed reap a golden harvest.

The technic of treatment is taken up in Chapter 7. The 100 patients treated and results obtained are discussed in Chapters 8 and 9. Thirty of the patients had hypertrophic arthritis, 38 hypertrophic spondylitis, 9 atrophic arthritis, 11 atrophic spondylitis, 2 "uric arthritis," 6 acromioclavicular arthritis, and 4 periarthritis calcarea. In the main the author was not only satisfied but enthusiastic with his results, which included relief of pain (sometimes "surprising" or even "truly remarkable") and reduction of effusion, stiffness, and swelling. Patients who had "uric arthritis" were regarded as being especially suitable for roentgen ray therapy, but why not, since acute gouty arthritis usually subsides spontaneously within a short time? In this day of seeming miracles achieved with the sulfonamides, the author dared to state (page 122) that gonorrheal arthritis is "perhaps the best indication for roentgen treatment," but he did not include any data thereon.

The summary of results and conclusions (Chapter 10) is interesting, but had better be taken with mental reservations. Physicians who have read more critical appraisals of roentgen therapy for arthritis (such as one from the Rackham Arthritis Research Unit of the University of Michigan: J. A. M. A. 116: 1995–2001, May 3, 1941) and those many clinicians and rheumatologists who have been disappointed with this form of therapy will consider the author guilty of unwarranted enthusiasm, which he has not justified by this presentation of his experience. No control studies of any sort were made. How important such studies are was revealed by the Michigan report alluded to, which showed that in most cases and types of arthritis (with spondylitis rhizomelica as the possible exception) supposed results from roentgen therapy were almost entirely, if not entirely, of psychogenic origin, since most patients obtained as much "relief" when roentgen therapy was deliberately administered with the roentgen rays entirely cut off from the joints by lead screens as they did when the joints were actually irradiated.

Despite its lack of comprehensiveness and the author's lack of critical judgment, this volume may serve as a useful introduction to the subject. Although it is unconvincing in its main theme, it may arouse further interest and stimulate better controlled studies of the subject. It certainly does not answer the clinician's query, "Is roentgen therapy really any good in arthritis? If so, how good and in what cases?"

The Employment of Physicians by Hospitals: Some Legal Aspects

(Continued from September issue)

The fact that benevolent corporations have been held not liable for the torts of employed physicians does not prove that such hospitals are not engaged in the practice of medicine. It simply proves they are not liable under the doctrine of *respondeat superior*. To these institutions the comment of the Restatement may be applied: "The normal status of a physician employed by one person to render medical services to another is that of an independent contractor, responsible to the master, not for the manner but only the results of his service."[52] But, obviously, he could not be an independent contractor in those cases holding the hospital liable for his negligence. When a charity patient is admitted for treatment to an eleemosynary institution, the physician's relation to the corporation employing him is analogous with his relation to the parent or guardian of a child, who engages his services for the child. It is simply the case of one person (for convenience the law resorts to a fiction and regards the corporation in certain matters as a person) obtaining and paying for services rendered by a physician to a dependent third party.

Under this theory, benevolent associations not operated for profit have been held not to be engaged in the practice of medicine by furnishing the services of physicians to members.[53] It is significant, however, that in most of these tort cases the question of agency has been circumvented by finding an implied waiver of liability by the beneficiary, or resorting to the trust fund theory.[54] Too, the "loaned servant" doctrine has been invoked to exempt charitable hospitals from liability for torts of its employees while assisting an attending physician or surgeon.[55]

Another line of cases to be distinguished from those holding a hospital corporation liable for the torts of its employees are those in which an employer or any third person has been held as not liable in an action of law for malpractice perpetrated by a physician whose fees are paid by the employer. Most railway physicians and industrial surgeons are to be found under this category. Here no profit ensues to the employer or to the third person. He does not charge the patient a fee; he merely agrees to pay for the services. Here the physician is an independent contractor, and not an agent or servant of the party paying for the services.[56]

Respondeat Superior.—From an examination of the cases pertaining to the liability of an incorporated hospital for the torts of its employed physicians, we are forced to the conclusion that where a corporation employs a physician at a fixed stipend and reaps a profit from the fees charged for his services, the corporation itself charging and collecting fees for the physician's services, an agency relationship is created and the familiar doctrine of *respondeat superior* applies.

Occupying the position of principal in an agency relationship, the hospital is subject to another maxim in the law: *Qui facit per alium, facit per se.* The hospital is engaged in the practice of medicine.

Where a hospital merely undertakes to supply rooms, board, hospital facilities, nursing services, and internes to act under the direction of the physician selected by the patient (loaned servant doctrine), the hospital is not practising medicine. Where the corporation merely procures a member of the staff to attend the patient and the physician is not in the employment of the corporation, the corporation is not practising medicine; the physician is an inde-

[52] *Restatement, op. cit.*, Sec. 223. See Yale L. J. 348, and cases cited there.

[53] 119 A. L. R. 1284.

[54] England v. Hosp. of the Good Samaritan, 16 Cal. App. (2nd) 640, 61 Pac. (2nd) 48 (1936); Hawthorne v. Blythewood, 118 Conn. 617, 174 Atl. 81 (1934); D'Amato v. Orange Memorial Hosp., 101 N. J. 127 Atl. 340; Mikota v. Sister of Mercy Hosp., 183 Iowa 1378, 168 N. W. 219 (1918); Rudy v. Lakeside Hosp., 155 Ohio St. 539, 155 N. E. 126 (1926); Bise v. St. Luke's Hosp., 181 Wash. 269, 43 Pac. (2nd) 4 (1935).

[55] Armstrong v. Wallace (Cal.) 37 Pac. (2nd) 467.

[56] Borgeas v. Oregon Short Line Ry. (Mont.) 236 Pac. 1069. ("The act of the servant becomes the act of the master, who has the right to control the manner in which he discharges his duties, and, when injury results, they are joint tortfeasors. But the relation of master and servant, or of principal and agent, does not exist between the railroad company as employer, and a surgeon employed to treat an injured employee, the reason being that the employer has no right to control the surgeon in the treatment of the case . . . ; and the rule of *respondeat superior* does not apply in the case of such employment.")

pendent contractor answerable to the patient alone. Likewise, where the physician is an employee of the corporation, but his services are gratuitous, the doctrine of *respondeat superior* is usually not applicable.[57] These are special circumstances resulting in a departure from the prevailing rule.

Corporate Practice.—Having applied the accepted maxims of agency, we have reached an affirmative answer to the first of the two questions presented in our opening: A hospital which employs a physician on a salary or other stipulated compensation, the hospital charging and collecting fees for the physician's services, is, according to the general authority, itself engaged in the practice of medicine. We turn now to the second question presented: Is such practice lawful?

In an almost unbroken line of cases, the courts have answered this question in the negative. The common law rule forbidding the practice of law by corporations was long ago extended to apply to medicine and allied professional fields.[58]

In the absence of express statutory authority, the weight of judicial reason and authority favors the view that neither a corporation nor any other unlicensed person or entity may engage in the unlicensed practice of medicine through licensed employees. The reason for the rule may be stated in general to be the inability of a corporation to possess the specified requirements; its incapacity to qualify by taking a personal examination; and the recognition that because of the inherent characteristics of a corporation there can never exist between it and the patient that confidential and intimate personal relationship ordinarily present between physician and patient.[59] A corporation cannot be licensed to practise medicine because it cannot satisfy the requirements of the pertinent medical practice act.[60] It cannot present evidence of educational or moral qualifications nor can it pass the required examinations given by the licensing board.[61]

Since a corporation cannot legally practise medicine directly, it cannot do so indirectly by means of agents duly licensed to practise.[62] After citing a few cases holding to the contrary,[63] the Bureau of Legal Medicine and Legislation of the American Medical Association states: "The influence of these cases, however, has been negative on courts subsequently passing on the right of a corporation to practise medicine. The Lewin case seems never to have been cited or referred to by a court of appellate jurisdiction. The Liggett case, in which the United States Supreme Court held unconstitutional a Pennsylvania statute requiring drug stores to be owned by licensed pharmacists only, has been ably and logically distinguished from the problem presently involved by the Supreme Court of Colorado in *People v. Painless Parker Dentist, 275 Pac. 928* and by the Supreme Court of Illinois in *People v. United Medical Service, Inc., 200 N. E. 157.*

"The Brown case in which the Supreme Court of Washington held unconstitutional a state statute forbidding any person other than a licensed dentist to own or operate a dental office, has been ignored in most of the more recent cases, has been expressly limited even in Washington (see *In re O'Neill, 41 Wash. 174*), and has been expressly repudiated by the Supreme Court of California in *Parker v.*

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[57] Coldwater v. Citizens Gas Co. (N. Y. Mun. Ct. 1938) 7 N. Y. S. (2nd).

[58] See 73 A. L. R. 1327 (1931) and cases cited there. (Optometry) 102 A. L. R. 334. State *ex rel.* Beck v. Goldman Jewelry Co., 142 Kans. 881; Funk Jewelry v. State (1935) (Ariz.) 50 Pac. (2nd) 945; Eisensmith v. Buhl Co. (1934) (W. Va.) 178 S. E. 695; Stern v. Flynn (1935) 154 Misc. 609, 278 N. Y. S. 598. (Medicine) See 103 A. L. R. 1240, and cases cited there. ("The majority, though not all, of the decisions on the subject, hold that neither a corporation nor any other unlicensed person or entity may engage in the practice of medicine, surgery, or dentistry through licensed employees.") 19 C. J. Sec. 402. See 119 A. L. R. 1290. *Cf.* Silver v. Lansburgh & Bros., *et al.* (D. C.) 27 F. Supp. 682, 111 F. (2nd) 518.

[59] McMurdo v. Getter (Mass.) 10 N. E. (2nd) 139.

[60] From a memorandum prepared by the Bureau of Legal Medicine and Legislation of the American Medical Association. The author wishes here to express his appreciation for the generous and valuable assistance rendered by Mr. T. V. MacDavitt and Mr. J. W. Holloway, Jr., acting director of that Bureau.

[61] People v. Painless Parker Dentist (Colo.) 275 P. 928; State v. Bailey Dental Co. (Iowa) 234 N. W. 260; People v. United Medical Service, Inc. (Ill.) 200 N. E. 157; Com. *ex rel.* Attorney General v. Alba Dentists Company, 13 Pa. D. R. 432.

[62] People v. John H. Woodbury Dermatological Institute (N. Y.) 85 N. E. 697; Hannon v. Siegel-Cooper Co. (N. Y.) 60 N. E. 597; People *ex rel.* Lederman v. Warden of City Prison (N. Y. S. 977; Granger v. Adson, *et al.* (Minn.) 250 N. W. 722; Winslow v. Kansas State Board of Dental Examiners, 14 Pac. (2nd) 67; People *ex rel.* State Board of Medical Examiners v. Pacific Health Corporation, Inc. (Cal.) 82 Pac. (2nd) 429; Benjamin Franklin Life Assur. Co. v. Mitchell Insurance Com'r. (Cal.) 58 Pac. (2nd) 984; Pacific Employers Ins. Co. v. Carpenter (Cal.) 52 Pac. (2nd) 992. State Board of Dental Examiners v. Walsh (Colo.) 8 Pac. (2nd) 704; State v. Williams (Ind.) 5 N. E. (2nd) 961.

[63] Memorandum *supra.* State *ex inf.* Sager v. Lewin (Mo.) 106 S. W. 581; Louis K. Liggett Co. v. Baldridge, Atty. General of Pa., 49 Sup. Ct. 57; State v. Brown (Wash.) 79 Pac. 635; State Electro-Medical Institute v. State (Neb.) 103 N. W. 1078; State-Electro Medical Institute v. Platner (Neb.) 103 N. W. 1079.

Board of Dental Examiners, 14 Pac. (2nd) 67. There the Supreme Court of California said:

"'Appellant claims that there is a distinction between the practice of dentistry which the statute undertakes to regulate and the purely business side of the practice; that the first requires skill and learning, while the latter requires only training in business transactions, and if the management or conduct of the "business side" by a layman is inhibited by statute, then the inhibitions of the statute are beyond the scope of the police power of the state, and are void as being unconstitutional, citing *State v. Brown, 37 Wash. 97, 79 Pac. 635.* . . . But we are not prepared to hold with the contention that a corporation or an unlicensed person may not be prevented from managing, conducting, or controlling what petitioner terms the "business side" of the practice of dentistry. The law does not assume to divide the practice of dentistry into that kind of departments. Either one may extend into the domain of the other in respects that would make such a division impractical if not impossible. The subject is treated as a whole . . .'

"The remaining cases that can be cited as authority for permitting a corporation to practise medicine are the two Nebraska cases involving State Electro-Medical Institute, *supra.* These cases have been expressly repudiated by the Supreme Courts of Colorado and Iowa, and no court of appellate jurisdiction has adopted their holding. The fallacious reasoning which the Nebraska court . . . employed is apparent. The court, while admitting that a corporation cannot be licensed to practise medicine, asserted that it was impossible for a corporation to practise, saying:

"'It is impossible to conceive of an impersonal entity "judging the nature, character and symptoms of the disease," or giving or prescribing the application of the remedy to the disease. Members of the corporation, or persons in its employ, might do these things, but the corporation itself is incapable to do them. The qualification of a medical practitioner is personal to himself. The intention of the law is that one who undertakes to judge the nature of a disease . . . must have certain personal qualifications; and, if he does these things without having complied with the law, he is subject to its penalties. Making contracts is not practicing medicine. Collecting the compensation therefor is not practicing medicine within the meaning of this statute. No professional qualifications are requisite for doing these things.'"

It is manifest that the Supreme Court of Nebraska, in reaching this conclusion, lost sight of the fact that a corporation is an intangible creature of the law that can act only through human agents, and that the acts of the agents are attributed to the corporation. For instance, a public service corporation does not by its intangible self directly maintain its power plant, distribute electricity, and operate its conveyances. The intangible corporation itself cannot perform these physical acts. It hires men to do them. Yet no one for a moment says that the "corporation" cannot and does not provide electricity and transportation. By no reasonable process of logic, then, can one say that a corporation employing licensed physicians to diagnose cases of illness and to treat them, is itself not practising medicine.

The principles stated above are as applicable to a corporation composed solely of licensed physicians as they are to any other corporation. A corporation is an entity separate and apart from its members. Its authority and power are derived solely from its charter and from pertinent state statutes. It derives no authority and no power by virtue of the qualifications of its component members. The fact that every member of a corporation is licensed to practise medicine does not endow that corporation with any authority to practise medicine. In this connection, with respect to the practice of law by a corporation composed solely of members of the Bar, an appellate court of California said in *People ex rel. Los Angeles Bar Assn. v. Calif. Protective Corporation, (1926) 76 Cal. App. 354, 244 Pac. 1089:*

"It is true that individuals who are duly licensed members of the bar may 'lawfully' associate themselves in any unincorporated form of association, such as a partnership, for the practice of law. But such individuals may not associate themselves for the practice of law under the aegis of a corporation. Though all the directors and officers of the corporation be duly licensed members of the legal profession, the practice of law by the corporation would be illegal, nevertheless. At any time those directors and officers, by death or by transfer of their shares, might be succeeded by laymen none of whom possessed the right to practice law."

An auto club was held to be practising law though a practically unlimited choice of attorneys was given the members.[64] Despite the fact that the Illinois statute prohibiting the corporate practice of law expressly provides that it does not apply to corporations not-for-profit, the rule has been applied to corporations organized not-for-profit and which were engaged in the practice of law.[65]

Notwithstanding the argument that the ethical considerations required by the medical profession are satisfied when the profit motive is eliminated as in the case of eleemosynary institutions, the personal relationship essential to good medical practice is impaired. One of

[64] *In re* Maclub of America (Mass.) (1936) 3 N. E. (2nd) 272.

[65] People v. Motorists' Assn. of Ill., 354 Ill. 595, 188 N. E. 827; People *ex rel.* Courtney v. Assn. of Real Estate Taxpayers, 354 Ill. 102, 187 N. E. 823; People v. Chicago Motor Club, 362 Ill. 50, 199 N. E. 1.

the best comments on this subject is that contained in *McMurdo v. Getter, (Mass.) 10 N. E. (2nd) 139,* which involved the unlawful practice of optometry. After discussing the licensing of certain businesses, the court said in part:

"... A different rule has been applied to the learned professions. These are characterized by the need of unusual learning, the existence of confidential relations, the adherence to a standard of ethics higher than that of the marketplace and in a profession like that of medicine by intimate and delicate personal ministration. Traditionally, the learned professions were theology, law and medicine; but some other occupations have climbed and still others may climb to the professional plane. . . . Dentistry, a branch of medicine, has done so within modern times. Professional men may be held to a higher ethical code, for example, by the restriction of advertising, than one engaged in ordinary business . . .. The rule is generally recognized that a licensed practitioner of a profession may not lawfully practice his profession among the public as the servant of an unlicensed person or corporation; and that, if he does so, the unlicensed person or corporation employing him is guilty of practicing that profession without a license. A corporation as such cannot possess the personal qualities required of a practitioner of a profession. Its servants, though professionally trained and duly licensed to practice, owe their primary allegiance and obedience to their employer, rather than to the clients or patients of their employer. The rule stated recognizes the necessity of immediate and unbroken relationship between a professional man and those who engage the services . . . . In the absence of statutory modifications in favor of hospitals or others . . . . the same rule (as to lawyers) applies to physicians and dentists."

The "Group Health" Case.—In the recent much discussed case of the Group Health Association in Washington,[66] the District of Columbia Court held that a corporation organized not for profit to engage in the practice of medicine was not in violation of the law. Said the court, "Such a corporation, not for profit but for the mutual benefit of its members, is in my opinion not engaged in the practice of medicine, or in holding itself out as doing so. It is true that a corporation can act only through its agents and employees, but the physicians with whom the plaintiff makes contract are rather in the position of independent contractors, and the plaintiff does not in any way undertake to control the manner in which they attend or prescribe for patients."

We have seen that the great weight of authority is contra.[67] We have likewise seen that the fact of control is not determining—it is the right of control, a right which invariably exists in the relationship of employer and employee. The courts have repeatedly asserted that the practice of a profession cannot be divided into departments, on one side performance of service, on the other management of the financial relationship.[68] The law has wisely refused to allow a third party to shift the allegiance of the practitioner from the patient to himself.

In commenting on the Group Health case Laufer, referring to the majority view, states: "Although the corporation's inability to act physically is recognized, the acts of its agents are attributed to it. The corporation is then treated as a human actor. Where the act is the practice of medicine, the corporation itself is said to practice and, being unlicensed, is held guilty of violating the Licensure Act. The flaw in this reasoning lies in its anthropomorphism."[69]

Here is the profound principle involved. The truth is that the whole philosophy of medicine is founded upon a spirit of anthropomorphism. Its concepts are, first and last, humanistic. Every consideration, legal, economic, or scientific, must be examined in terms of its human values—of its application to the welfare of a single human being, the patient.

The science and the ethics of medicine did not spring from the marketplace. They were born in the temple of Aesculapius and nurtured in the individual hands of many generations of physicians. The sufferings of a sick man can be relieved only by the ministrations of another man—the physician. The corporation, so convenient for modern-day business, is alien to the personal and intimate relationship which surrounds the care of the sick and dying.

The doctrine forbidding the practice of medicine by corporations has found expression in our system of jurisprudence under the sound reasoning that the interjection of a third party between a doctor and his patient destroys the close relationship so important in the treatment of sickness. As with other settled principles in the law, it is founded upon considerations for the benefit of mankind and the welfare of our society.

MAC F. CAHAL

Executive Secretary,
American College of Radiology

[66] Group Health Assn. v. Moor (D. C.) (1938) 24 F. Supp. 445, 107 Fed. (2nd) 703. See "The American Medical Association and the Anti-Trust Laws," 8 Fordham L. R. 1, Jan. 1939, p. 82.

[67] *Supra.*, footnote 58.

[68] Parker v. Board of Dental Examiners, 216 Cal 285, 14 Pac. (2nd) 67; Dr. Allison, Dentist, Inc. v. Allison, 360 Ill. 368, 196 N. E. 799. ("A corporation cannot qualify to practice a learned profession, since it can have neither honesty nor conscience and its loyalty must be rendered to its managers, directors, and stockholders.")

[69] Laufer, Joseph, *Law and Contemporary Problems,* Duke University School of Law, Vol. VI, No. 4, Autumn, 1939, p. 525.

RADIOLOGICAL SOCIETIES OF NORTH AMERICA

Editor's Note.—Will secretaries of societies please cooperate with the Editor by supplying information to keep these notices accurate and up to date? Please send information to Howard P. Doub, M.D., Henry Ford Hospital, Detroit, Mich.

UNITED STATES

Radiological Society of North America.—Secretary, D. S. Childs, M.D., 607 Medical Arts Building, Syracuse, N. Y. Annual Meeting, Dec. 1–5, 1941, San Francisco, Calif.

American Roentgen Ray Society.—Secretary, C. B. Peirce, Royal Victoria Hospital, Montreal, Canada.

American College of Radiology.—Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago, Ill. Annual Meeting, 1942, Atlantic City, N. J.

Section on Radiology, American Medical Association.—Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual Meeting, 1942, Atlantic City, N. J.

CALIFORNIA

California Medical Association, Section on Radiology.—Secretary, Joseph D. Coate, M.D., 434 Thirtieth St., Oakland.

Los Angeles County Medical Association, Radiological Section.—Secretary, Wilbur Bailey, M.D., 2007 Wilshire Blvd.; Meets second Wednesday of each month at County Society Building.

Pacific Roentgen Society.—Secretary-Treasurer, L. Henry Garland, M.D., 450 Sutter St., San Francisco. Society meets annually during annual meeting of the California Medical Association.

San Francisco Radiological Society.—Secretary, J. Maurice Robinson, M.D., University of California Hospital. Meets monthly on third Thursday at 7:45 P.M., for the first six months at Toland Hall (University of California Medical School) and for the second six months at Lane Hall (Stanford University School of Medicine).

COLORADO

Denver Radiological Club.—Secretary, Paul R. Weeks, M.D., 520 Republic Bldg. Meets third Friday of each month at homes of members.

CONNECTICUT

Connecticut State Medical Society, Section on Radiology.—Secretary-Treasurer, Max Climan, M.D., 242 Trumbull St., Hartford. Meetings bimonthly, on second Thursday. Place of meeting selected by Secretary.

FLORIDA

Florida Radiological Society.—Secretary-Treasurer, Elliott M. Hendricks, M.D., 314 Sweet Bldg., Fort Lauderdale. The next meeting will be at the time of the annual meeting of the Medical Association of Florida in the spring.

GEORGIA

Georgia Radiological Society.—Secretary-Treasurer, Robert C. Pendergrass, M.D., Prather Clinic Bldg., Americus. Meetings twice annually, in November and at the annual meeting of the Medical Association of Georgia in the spring.

ILLINOIS

Chicago Roentgen Society.—Secretary, Chester J. Challenger, M.D., 3117 Logan Blvd. The Society meets at the Palmer House on the second Thursday of October, November, January, February, March, and April.

Illinois Radiological Society.—Secretary-Treasurer, William DeHollander, M.D., St. Johns' Hospital, Springfield. Meetings quarterly by announcement.

Illinois State Medical Society, Section on Radiology.—Secretary, Earl E. Barth, M.D., 303 E. Chicago Ave., Chicago.

INDIANA

The Indiana Roentgen Society.—Secretary-Treasurer, Harold C. Ochsner, Methodist Hospital, Indianapolis. Annual meeting in May.

IOWA

The Iowa X-ray Club.—Holds luncheon and business meeting during annual session of Iowa State Medical Society.

KENTUCKY

Kentucky Radiological Society.—Secretary-Treasurer, Joseph C. Bell, M.D., 402 Heyburn Bldg., Louisville. Meeting annually in Louisville, third Sunday afternoon in April.

LOUISIANA

Louisiana Radiological Society.—Secretary-Treasurer, Johnson R. Anderson, M.D., North Louisiana Sanitarium, Shreveport. Meets annually at same time as State Medical Society. Next meeting, New Orleans, April 1942.

Shreveport Radiological Club.—Secretary-Treasurer, W. R. Harwell, M.D. Meetings monthly on the second Wednesday, at the offices of the various members.

MARYLAND

Baltimore City Medical Society, Radiological Section.—Secretary, Walter L. Kilby, M.D., 101 W. Read St. Meetings are held the third Tuesday of each month.

MICHIGAN

Detroit X-ray and Radium Society.—Secretary-Treasurer, E. R. Witwer, M.D., Harper Hospital, Detroit. Meetings first Thursday of each month from October to May, inclusive, at Wayne County Medical Society club rooms, 4421 Woodward Ave., Detroit.

Michigan Association of Roentgenologists.—Secretary-Treasurer, J. E. Lofstrom, M.D., St. Mary's Hospital, Detroit. Meetings quarterly by announcement.

MINNESOTA

Minnesota Radiological Society.—Secretary, John P. Medelman, M.D., 572 Lowry Medical Arts Bldg., St. Paul. Meetings quarterly.

MISSOURI

The Kansas City Radiological Society.—Secretary, P. E. Hiebert, M.D., 907 North Seventh St. (Huron Bldg.), Kansas City, Kansas. Meetings last Thursday of each month.

The St. Louis Society of Radiologists.—Secretary, Wilbur K. Mueller, M.D., University Club Bldg. Meets on fourth Wednesday of October, January, March, and May, at a place designated by the president.

NEBRASKA

Nebraska Radiological Society.—Secretary, D. A. Dowell, M.D., 816 Medical Arts Bldg., Omaha. Meetings third Wednesday of each month at 6 P.M. in either Omaha or Lincoln.

NEW ENGLAND

New England Roentgen Ray Society (Maine, New Hampshire, Vermont, Massachusetts, and Rhode Island).—*Secretary,* Hugh F. Hare, M.D., Lahey Clinic, Boston, Mass. Meets monthly on third Friday at Boston Medical Library.

NEW JERSEY

Radiological Society of New Jersey.—Secretary, H. J. Perlberg, M.D., Trust Co. of New Jersey Bldg., Jersey City. Meetings at Atlantic City at time of State Medical Society and midwinter in Newark as called by president.

NEW YORK

Associated Radiologists of New York, Inc.—Secretary, William J. Francis, M.D., 210 Fifth Ave., New York City. Regular meetings the first Monday evening of the month in March, May, October, and December.

Brooklyn Roentgen Ray Society.—Secretary-Treasurer, Leo Harrington, M.D., 880 Ocean Ave. Meetings held the fourth Tuesday of every month, October to April.

Buffalo Radiological Society.—Secretary-Treasurer, Joseph S. Gianfranceschi, M.D., 610 Niagara St. Meetings second Monday evening each month, October to May, inclusive.

Central New York Roentgen Ray Society.—Secretary-Treasurer, Carlton F. Potter, M.D., 425 Waverly Ave., Syracuse. Meetings are held in January, May, and October, as called by Executive Committee.

Long Island Radiological Society.—Secretary, Marcus Wiener, M.D., 1430 48th St., Brooklyn. Meetings fourth Thursday evening each month at Kings County Medical Bldg.

New York Roentgen Society.—Secretary, Paul C. Swenson, M.D., Presbyterian Hospital, New York, N. Y.

Rochester Roentgen-ray Society.—Secretary, S. C. Davidson, M.D., 277 Alexander St. Meetings at convenience of committee.

NORTH CAROLINA

Radiological Society of North Carolina.—Secretary-Treasurer, Major I. Fleming, M.D., 404 Falls Road, Rocky Mount. Meeting with State meeting in May, and meeting in October.

NORTH DAKOTA

North Dakota Radiological Society.—Secretary, L. A. Nash, M.D., St. John's Hospital, Fargo. Meetings by announcement.

OHIO

Ohio Radiological Society.—Secretary, J. E. McCarthy, M.D., Cincinnati. The next meeting will be held at the time and place of the annual meeting of the Ohio State Medical Association.

Cleveland Radiological Society.—Secretary-Treasurer, J. O. Newton, M.D., 13921 Terrace Road, East Cleveland. Meetings at 6:30 P.M. at the Mid-day Club, in the Union Commerce Bldg., on fourth Monday of each month from October to April, inclusive.

Radiological Society of the Academy of Medicine (Cincinnati Roentgenologists).—*Secretary-Treasurer,* Justin E. McCarthy, M.D., 707 Race St. Meetings held third Tuesday of each month.

PENNSYLVANIA

Pennsylvania Radiological Society.—Secretary-Treasurer, L. E. Wurster, M.D., 416 Pine St., Williamsport. The Society meets annually; time and place of next meeting will be announced later.

The Philadelphia Roentgen Ray Society.—Secretary, Barton R. Young, M.D., Temple University Hospital, Philadelphia. Meetings held first Thursday of each month at 8:15 P.M., from October to May, in Thomson Hall, College of Physicians, 21 S. 22nd St., Philadelphia.

The Pittsburgh Roentgen Society.—Secretary-Treasurer, Harold W. Jacox, M.D., 4800 Friendship Ave., Pittsburgh, Pa. Meetings are held on the second Wednesday of each month at 4:30 P.M., from October to June, at the Pittsburgh Academy of Medicine, 322 N. Craig St.

ROCKY MOUNTAIN STATES

Rocky Mountain Radiological Society (North Dakota, South Dakota, Nebraska, Kansas, Texas, Wyoming, Montana, Colorado, Idaho, Utah, New Mexico).—*Secretary,* A. M. Popma, M.D., 220 North First St., Boise, Idaho.

SOUTH CAROLINA

South Carolina X-ray Society.—Secretary-Treasurer, Malcolm Mosteller, M.D., Columbia Hospital, Columbia. Meetings in Charleston on first Thursday in November, also at time and place of South Carolina, State Medical Association.

TENNESSEE

Memphis Roentgen Club.—Chairmanship rotates monthly in alphabetical order. Meetings second Tuesday of each month at University Center.

Tennessee Radiological Society.—Secretary-Treasurer, Franklin B. Bogart, M.D., 311 Medical Arts Bldg., Chattanooga. Meeting annually with State Medical Society in April.

TEXAS

Texas Radiological Society.—Secretary-Treasurer, L. W. Baird, M.D., Scott and White Hospital, Temple. Meets annually.

VIRGINIA

Virginia Radiological Society.—Secretary, Charles H. Peterson, M.D., 603 Medical Arts Bldg., Roanoke.

WASHINGTON

Washington State Radiological Society.—Secretary-Treasurer, Kenneth J. Holtz, M.D., American Bank Bldg., Seattle. Meetings fourth Monday of each month at College Club, Seattle.

WISCONSIN

Milwaukee, Roentgen Ray Society.—Secretary-Treasurer, Irving I. Cowan, M.D., Mount Sinai Hospital, Milwaukee. Meets monthly on first Friday at the University Club.

Radiological Section of the Wisconsin State Medical Society.—Secretary, Russel F. Wilson, M.D., Beloit Municipal Hospital, Beloit. Two-day annual meeting in May and one day in connection with annual meeting of State Medical Society, in September.

University of Wisconsin Radiological Conference.—Secretary, E. A. Pohle, M.D., 1300 University Ave., Madison, Wis. Meets every Thursday from 4 to 5 P.M., Room 301, Service Memorial Institute.

CANADA

Section on Radiology, Canadian Medical Association.—Secretary, W. J. Cryderman, M.D., Medical Arts Bldg., Toronto.

Section on Radiology, Ontario Medical Association.—Secretary, W. J. Cryderman, M.D., 474 Glenlake Avenue, Toronto.

Canadian Association of Radiologists.—Honorary Secretary-Treasurer, A. C. Singleton, M.D., Toronto.

La Société Canadienne-Française d'Eléctrologie et de Radiologie Médicales.—General Secretary, Origène Dufresne, M.D., Institut du Radium, Montreal. Meetings are held the third Saturday of each month, generally at the Radium Institute, 4120 East Ontario Street, Montreal; sometimes, at homes of members.

CUBA

Sociedad de Radiología y Fisioterapia de Cuba.—Offices in Hospital Mercedes, Havana. Meetings are held monthly.

ABSTRACTS OF CURRENT LITERATURE

ROENTGEN DIAGNOSIS

The Head and Neck

The Chest

The Digestive Tract

The Skeletal System

RADIOTHERAPY

Malignant Conditions

Non-Malignant Conditions

Reactions to Radiation

ROENTGEN DIAGNOSIS

HEAD AND NECK

Researches on Cerebral Arteriography. Giacomo Galletto. Radiol. med. **27:** 905–917, December 1940.

In a well written and well illustrated article Galletto reports his researches on arteriography of the cerebrum. His work was all done on the cadaver. His principal aim was to study the behavior of different contrast media when injected into the cerebral arteries and the cerebral spaces (such as the ventricles), and particularly to see if there were any advantages to be obtained by injecting the arteries and the spaces simultaneously. He also sought to determine the influence, if any, of hypertension, artificially provoked by injection of the contrast media into the ventricles or arteries, on the resultant arterioroentgenogram. His chief conclusions were as follows: The best results are obtained by injecting thorotrast into the internal carotid and vertebral arteries at the same time and under pressure. When the liquid is injected simultaneously into the arteries and subdural spaces, sometimes only one of the cerebral hemispheres becomes visible.

A. MAYORAL, M.D

The Sella Turcica in Various Types of Mental Disease. D. Agati. Arch. di radiol. **16:** 5–23, January–February 1940.

The author made a roentgen study of the skull in 196 patients with various mental diseases and 29 persons who were more or less normal. In the first group he found 51 cases of fused clinoids. He discusses the possible relationship between this anatomical finding and endocrine balance. Among the rare conditions encountered were a bony bridge from one side of the tuberculum sellae to the quadrilateral plate in one patient, two cases of dorsum elongatum, and one case of segmentation of the dorsum sellae.

E. T. LEDDY, M.D.

THE CHEST

Mass Radiography of the Chest. S. C. Shanks. Brit. J. Radiol. **14:** 45–53, February 1941.

Miniature radiography of the chest, by photographing the image on a fluorescent screen, is the most effective way of surveying large numbers of subjects. Full-sized radiography is too expensive; fluoroscopy is cheap but requires the constant attention of an expert. Films can be made by the miniature method by trained technicians and read at leisure by experts.

Three types of apparatus are briefly described, and the combined radiographic and photographic technics of several workers are summarized. With an $f/1.5$ stop, the radiographic exposures vary between 60 and 100 kv., 80 to 100 ma., with an exposure time of 0.2 to 0.5 seconds.

The organization of a four-man team to make the surveys is described. As cooperation of the patient is necessary for successful radiography, he is rehearsed on a dummy apparatus. SYDNEY J. HAWLEY, M.D.

Comparison of Photofluorograms and Regular Large Films during Serial Examination of Workers Exposed to Dust. E. Saupe. Fortschr. a. d. Geb. d. Röntgenstrahlen **62:** 145–159, September 1940.

This paper is based on the examination of 25,000 workers in the mining and ceramic industries of Saxony and the adjacent Sudeten countries. Comparisons were made not only in cases demonstrating pathologic conditions with the photofluorographic method, but also in a number of cases where this method revealed no evidence of disease. It was found that a second-degree silicosis can be demonstrated by the photofluorographic method without difficulty. Less severe degrees of pneumoconiosis, however, offer increasing difficulty, and the analysis of silico-tuberculosis was found decidedly more difficult than from the study of full-sized films. Ambiguous reports—for instance, such statements as exaggerated hilar markings, accentuated and fuzzy pulmonary markings, faint mottling, etc.—cannot be eliminated completely. The photofluorographic method was regarded as unsatisfactory for the study of asbestosis; even the very best full-sized films could be regarded as barely sufficient for the study of this disease. Numerous diagnostic and technical details are discussed, as for instance, the evaluation of shadows created by superimposition of strata, apical changes, infiltrations located in lateral and basal areas, the differentiation between calcifying foci and blood vessels projected on end, etc. It is emphasized that one should not attempt to diagnosis on a technically insufficient record.

Evaluation of photofluorograms of workers exposed to dust requires more time and greater experience than surveys of "normal populations." The photofluorographic method is regarded as decidedly valuable, though many times it must be supplemented by additional regular film exposures. H. A. JARRE, M.D.

Diagnosis and Treatment of Tuberculosis. J. C. Koerth, H. P. Thomas, and J. M. Donaldson. Dis. of Chest **7:** 7–17, January 1941.

This article, written in a somewhat popular fashion for the general practitioner of medicine, emphasizes the physician's and the patient's responsibility for the delayed diagnosis of tuberculosis. An outline is given of the common symptoms and signs and the use of x-ray examination and other special examinations in diagnosis. WM. H. GILLENTINE, M.D.

Primary Carcinoma of the Lung in the Chinese. C. K. Hsieh, S. H. Wang, and Fa-Chu Chang. Chinese M. J. **58:** 381–407, October 1940.

The records for the past twenty years in the Peiping Union Medical College Hospital included 37 cases diagnosed as primary carcinoma of the lung. Twenty-two cases were confirmed pathologically, of which 18 occurred in Chinese patients. The increased incidence of this condition since 1921 roughly parallels the increased diagnosis of carcinoma generally, the difference being explained by the greater attention paid to the possibility. Judging by the case histories, diagnosis was made late in the disease. An excellent summary of roentgen and bronchoscopic methods of diagnosis is presented. The lesions are divided into central and peripheral types for ease of discussion and the distortion of structure in the two locations is made clear.

WM. H. GILLENTINE, M.D.

Differential Diagnosis of Rounded, Well Delineated Shadows in the Region of the Pulmonary Conus. Franz Eggs. Fortschr. a. d. Geb. d. Röntgenstrahlen **62:** 188-195, September 1940.

Four cases of rounded areas of density in the region of the pulmonary conus are reported, representing (1) delayed closure of the ductus arteriosus; (2) aneurysmal dilatation of the pulmonary artery and its branches, in all probability associated with atrial septal defect; (3) aneurysm of the left atrium; (4) aneurysm of the aortic arch. The differential diagnosis is discussed in view of the clinical manifestations.

H. A. JARRE, M.D.

Extrapleural Pneumothorax: Report of Experiences and Present Day Indications. Richard H. Overholt. Dis. of Chest **7:** 80–87, March 1941.

Extrapleural pneumothorax was attempted on 48 patients with pulmonary tuberculosis, 34 of whom were regarded as hopeless. The 47 patients surviving operation were observed for a period of time averaging twenty-one months for the group. Thirty-eight per cent were dead, 19 per cent were living with active disease, and 43 per cent were living with inactive disease at the end of this period. Extrapleural pneumothorax was continued in only 14 of the original 47 patients. In others treatment was continued by oleothorax, or conversion to thoracoplasty; in 2 no further treatment was given. Empyema occurred in 14 of the 51 spaces created. A broncho-extrapleural fistula was an important factor in the death of 7 patients. It was occasionally difficult to maintain collapse at the proper level by air refill. In 26 per cent, the sputum did not become negative. Extension of disease frequently necessitated operative enlargement of the cavity.

The author believes that the indications for extrapleural pneumothorax are limited. Today 22 of the original 48 patients would be advised to have the more diseased side attacked by primary thoracoplasty, producing a selective apical collapse. Extrapleural pneumothorax is now limited to cases unsuitable either for bilateral thoracoplasty or for unilateral thoracoplasty combined with some other type of collapse of the contralateral lung. WM. H. GILLENTINE, M.D.

Spontaneous Pneumothorax of the Newly Born, with Report of a Case. Wm. H. Wood, Jr., and W. H. Paine. Virginia M. Monthly **68:** 148–151, March 1941.

Spontaneous pneumothorax of the newborn is a rather rare condition. Its early recognition and treatment are of great importance, as the mortality is much higher than in older persons, in whom the vital processes of life are better established.

Twenty-two cases, including the present one, appear in the literature. As to the mechanism, there are several possibilities: ruptured subpleural blebs, interstitial emphysema of the lungs with extension along the fascial planes to the mediastinum and rupture of the mediastinal wall into the pleural cavity, rupture of congenital fluid or air cysts.

Diagnosis is best made with the x-ray. Clinically there may be nothing abnormal in the respiration, but usually there is some slight respiratory embarrassment with occasional sudden attacks of respiratory and circulatory difficulty.

Treatment consists of oxygen or carbon dioxide inhalations and aspiration of the pleural air, if necessary.

The case reported was of an otherwise normal child, of normal birth from a healthy mother. Nembutal and hyoscine obstetrical analgesia was used. The baby was cyanotic at first, but soon breathed well and appeared normal. It became slightly cyanotic after breast feeding, and oxygen and carbon dioxide inhalations were begun and continued intermittently. Physical examination revealed distant breath sounds, an impaired percussion note, and crepitant râles on the left.

The roentgen film showed a large right-sided pneumothorax with considerable compression of the left lung and displacement of the heart and mediastinum toward the left. Following aspiration of 40 c.c. of air from the right hemithorax, the position of the heart was improved and respiration was easier. Difficulty was again experienced during nursing, however, and a 20-gauge needle was filed off and left inserted between the third and fourth ribs anteriorly, held in place with adhesive tape. The other end was kept under water. Further efforts were unavailing and the child died.

At autopsy several emphysematous blebs were found over the surface of both lungs, but none was ruptured. No other abnormality was noted. The lungs had been aerated. There was considerable fat-like material in the bronchial tree. JOHN E. WHITELEATHER, M.D.

Factors in the Reduction of Mortality from Pulmonary Abscess. R. H. Overholt and W. R. Rumel. New England J. Med. **224:** 441–453, March 13, 1941.

Despite the advances of modern medicine the high mortality from lung abscess has changed but little and the usual advice of authorities to treat the condition conservatively brings the patient to a state of general debility rendering the prospect of a successful operative venture doubtful.

In a group of 19 cases treated by the authors in the conservative manner, the mortality rate was 53 per cent and the cure rate 26 per cent. Among 13 cases with lung resection, the mortality rate was 23 per cent and the cure rate 62 per cent. Those treated in an advanced stage by external drainage, numbering 28, showed a mortality rate of 32 per cent and cure rate of 26 per cent, while among 35 treated by early external drainage the mortality rate was 6 per cent and the cure rate 94 per cent.

Great value is placed upon accurate roentgen localization of the abscess cavity, its extent, and proximity to the chest wall. Views at various angles and positions are desirable rather than stereoscopic pairs. The main object is to determine the area of pleural symphysis through which drainage is performed.

The area of pneumonitis surrounding a lung abscess is dangerous to traverse and in drainage this region is to be avoided if at all possible, since the mortality rate increase has been found to be 300 per cent where this area is invaded surgically.

The simple lung abscess is contrasted with the complicated one, wherein daughter abscesses, bronchiectatic dilatations, or fibrosis are present, increasing the difficulty of operation and the mortality rate.

The operative procedure and the handling of complications are discussed in great detail. The advantage of early over delayed surgical attack is emphasized and the decreased mortality rate demonstrated.

JOHN MCANENY, M.D.

Surgical Treatment of Acute Pulmonary Abscess. Harold Neuhof. Dis. of Chest **7:** 74–79, March 1941.

The author discusses the pathology of the putrid or anaerobic and non-putrid or aerobic form of pulmonary abscess. His experience indicates that in either type the greatest success from operation is obtained when the pathology is that of a solitary monolocular lesion situated superficially within a pulmonary lobe, the overlying shell of lung tissue being thin and soft, compressed, and essentially avascular. In 109 consecutive cases operated upon by the author or Dr. Touroff during the past fifteen years, the mortality was 3.6 per cent. Rabin's method of localizing the abscessed cavity, by injecting into the musculature of one intercostal space a small amount of admixed lipiodol and methylene blue at the suspected site of contact of the abscess with the chest wall, followed by a series of plates taken in appropriate position, is vital to the success of operation. The cavity is entered through the overlying pleural adhesions—to avoid contamination of the pleural cavity—unroofed, and packed in a one-stage procedure. Operation in the author's series has resulted in cure in the great majority of cases in spite of the fact that one-third were of the severe or hyperacute variety. The imperative and elective indications for surgery, recognized by the author, are well chosen.

WM. H. GILLENTINE, M.D.

THE DIGESTIVE TRACT

Carcinoma of the Esophagus Developing in Benign Stricture. E. B. Benedict. New England J. Med. **224:** 408–412, March 6, 1941.

In a review of the literature, 33 cases of carcinoma of the esophagus were found arising in benign strictures, 16 of which resulted from lye burns. Two cases of esophageal carcinoma developing in benign strictures are presented here. The prognosis is the same as for any other esophageal carcinoma.

JOHN MCANENY, M.D.

Surgical Significance of Gastro-Intestinal Bleeding. Verne C. Hunt. Rocky Mountain M. J. **38:** 196–201, March 1941.

In 85 per cent of the cases of gastro-intestinal bleeding the source is an ulcer, either in the duodenum or in the stomach. Bleeding duodenal ulcer was found by Rivers and Wilbur, in a large series of cases, to account for approximately 60 per cent of all such hemorrhage, and in an additional 25 per cent gastric or postoperative anastomotic ulcers were responsible. Among other intragastric causes of hemorrhage are carcinoma, benign tumors, polyps, and erosion of the gastric mucosa in certain cases of esophageal hiatus hernia. It is the author's experience that once a peptic ulcer bleeds, the hemorrhage tends to recur.

Death occurs in 10 to 15 per cent of cases in which massive hemorrhage takes place. The danger of a fatal hemorrhage increases with age, being much higher in patients over fifty. Acute massive hemorrhage which subsides following the institution of non-surgical methods may occasion no great alarm for the moment; this is, of course, not the case if the hemorrhage shows little response to medical measures.

A policy followed by the author for years, considered by him to be free from uncertainty, embraces the following principles:

(1) Early and repeated transfusion of blood restores circulatory volume.

(2) Operation is seldom indicated under the age of fifty.

(3) Recurrence of massive hemorrhage two or more times in patients under fifty warrants surgical intervention as soon as the patient's condition will permit.

(4) Surgery is advised for patients over fifty when they have shown no improvement as the result of repeated or continuous transfusion in twelve to twenty-four hours.

(5) In patients over fifty who have recovered from a massive hemorrhage through the employment of non-surgical measures fate is not tempted, but surgery is advised.

(6) A direct operation is performed with excision of the lesion.

In hemorrhage from esophageal varices, the author has ligated the left coronary vein with excellent results.

The triad of obstructive jaundice, indeterminate bleeding, and intractable diarrhea may suggest a carcinoma of the papilla of Vater.

Ulceration in a Meckel's diverticulum in not an infrequent source of massive intestinal hemorrhage. Hemangiomatous lesions of the small intestine may cause hemorrhage. Such a lesion was recently seen by the author in the jejunum. He mentions, also, a case of hemangioma involving the sigmoid, rectum, and uterus, with recurrent hemorrhage over a long period of years.

PERCY J. DELANO, M.D.

Duodenal Diverticula and Their Complications with Particular Reference to Acute Pancreatic Necrosis. Robertson F. Ogilvie. Brit. J. Surg. **28:** 362–379, January 1941.

The 4 cases reported here show that a perivaterine diverticulum may produce definite obstruction of the pancreatic duct and that the association of acute pancreatic necrosis with a perivaterine diverticulum is probably neither vague nor accidental, but that these conditions may reasonably be related as effect and cause through this very factor of duct obstruction. In the first case the diverticulum was found in the second portion of the duodenum medial to and above the ampulla of Vater, and separated from the latter by only a thin mucous fold. Both the pancreatic and common bile ducts were dilated from obstruction by the diverticulum with resultant atrophy of the pancreas and death from obstructive jaundice. The other 3 cases also terminated fatally and postmortem examination revealed a diverticulum of the second portion of the duodenum associated with acute pancreatic necrosis.

Complications of duodenal diverticula include obstruction and diverticulitis. Obstruction may be further classified as (*a*) obstruction of the duodenum, (*b*) obstruction of the common bile duct, and (*c*) obstruction of the pancreatic duct. Diverticulitis is a rare complication, due to sterility of the diverticular contents, their retroperitoneal situation, their inverted position, and the usually wide-mouthed character of their ostium, which together tend to effect drainage into the bowel. Diverticulitis may in turn lead to one or other of several sequelae: perforation, peridiverticulitis, duodenitis, and cholangitis.

In one case of the reported series a calculus was found in the duodenal pouch. Gallstones are rare occurrences. One case of carcinoma occurring at the mouth of the pouch was reported.

MAX CLIMAN, M.D.

Metastasizing Argentaffine Tumor of the Cecum in a Case of Multiple Colonic Malignancies. Charles W. Mayo and William D. Wilson. Minnesota Med. **24:** 178–179, March 1941.

Although there are a great many reports in the literature concerning carcinoid tumors of the appendix, tumors of this type occurring elsewhere in the gastro-intestinal tract are relatively rare. Evidence of extension from the site of origin of these tumors is even less commonly encountered. Wyatt, in 1938, reported a cast of "multicentric carcinoid" of the cecum in which the tumor had metastasized to the liver (Ann. Surg. **107:** 260, 1938).

Including the case of Wyatt, only 9 examples of this type of tumor of the large bowel have been reported, and of these 3 have been found to have either local or distant metastases. Of the carcinoid tumors of the appendix, only 5 have been found to extend beyond the organ itself. Among small intestinal carcinoids extension has been reported in 36.

A case seen at the Mayo Clinic is reported. The patient was a white woman, fifty-five years of age, complaining of pain in the left lower quadrant of the abdomen of about three and a half years' duration. On two or three occasions she had passed bright red blood per rectum. Proctoscopic examination showed a polypoid tumor 10 cm. above the dentate margin, involving the left and posterior walls of the rectum. The lesion extended for 16 cm. proximal to this point. Biopsy showed adenocarcinoma, grade 1.

At operation the tumor was found as anticipated from proctoscopic examination. In addition, there was a small mass in the cecum about the size of a golf ball, close to the ileocecal valve, accompanied by palpable nodes in the mesentery. It was felt that this lesion was undoubtedly another carcinoma. Accordingly, a portion of the right half of the colon was resected and an end-to-side ileotransverse colonic stoma was made. Single-barreled colostomy, after the method of Lahey, was also performed, so that in the future the second part of a two-stage abdomino-perineal resection could be accomplished.

On gross pathologic examination of the cecum, the tumor was found to be about 4 cm. in diameter, presenting a characteristic orange-colored appearance on cut section. It was situated approximately half an inch from the base of the appendix, and that rudiment was not involved. On histopathologic examination it was found to be an adenocarcinoma, grade 2, of the "carcinoid" type, with involvement of the regional lymph nodes. The cells contained granules which reduced silver. Pathologic examination of the tissue removed from the rectum showed the tumor situated there to be polypoid carcinoma, grade 1, without node involvement.

It is generally conceded at present that the so-called carcinoid tumors arise from the Kultschitzky cells which are found in the base of the crypts of Lieberkühn. The ability of the cells of this tumor to reduce silver provides the surgeon with a positive means of diagnosis. On gross examination the yellow color of the tumor may given a hint as to its character.

Although there are those who still deny the malignancy of "carcinoid" tumors, it becomes increasingly apparent that they actually are true carcinomas.

PERCY J. DELANO, M.D.

Demonstration of Non-Opaque Stones in Fistulae between the Duodenum and Biliary System. A. Beutel. Fortschr. a. d. Geb. d. Röntgenstrahlen **62:** 247–252, October 1940.

Experience has shown that the majority of fistulae between the duodenum and biliary system develop as a result of perforation by biliary calculi. The demonstration of gas in the bile ducts must be regarded as highly suggestive of the presence of a fistula. In such instances, a careful search for opaque and non-opaque calculi and an attempt at demonstration of the fistula are indicated. Filling of the bile ducts through a fistula can often be enforced by prolonged right-sided Trendelenburg position, eventually with compression of the inferior horizontal duodenal segment. After filling of the biliary ducts gradual evacuation is induced, preferably through protracted walking exercises. Repeated roentgenologic exploration during this period of evacuation will frequently demonstrate the condition of the biliary ducts at the site of the fistula and reveal non-opaque biliary calculi after they have become coated with barium. Such a demonstration is of importance for the planning of therapeutic and surgical management. Two case reports illustrate observations possible under such conditions.

H. A. JARRE, M.D.

THE SKELETAL SYSTEM

Vertebral Compression Fractures Sustained during Convulsions. Serge Androp, Ellis S. Margolin, Joseph H. Marshall, and Miriam Rittenhouse. Arch. Surg. **42:** 550–556, March 1941.

The authors originally made a practice of studying roentgenographically only those patients treated by convulsive therapy in whom symptoms were present, but lately routine pre-convulsive and post-convulsive roentgenograms have been made. In 30 cases 7 instances of vertebral compression fracture were observed, 6 in men and 1 in a woman. All these patients were between the ages of twenty-eight and fifty years. Six were diagnosed as schizophrenics and one had a manic-depressive psychosis. Between 7 and 20 injections of metrazol were given per patient. In 3 cases no symptom suggestive of fracture was present; in 3 there were local tenderness and pain radiating along the nerve roots, lasting from three days to two weeks; 1 patient had discomfort lasting over a year, requiring the wearing of a support.

Similar fractures have been reported in tetanus and epilepsy, but from a review of the literature they seem to be relatively rare, a study of 50 patients having frequent severe grand-mal seizures failing to show any with fracture.

The site of fracture was most commonly from the 4th to the 8th thoracic vertebra, as contrasted with ordinary traumatic compressions, which are more common in the last thoracic and upper two lumbar vertebrae. The usual symptoms are tenderness and pain radiating along the nerve distribution. The cause of these fractures has been said to be restraint, but no restraint was used on any patient in this series. The treatments were given in bed with protection against direct injury of the spine. No known background of metabolic disease or skeletal defect was present. Age is not a factor. The predisposing causes are not known. Fractures may be of any degree of severity.

While the mechanism of fracture is not known, muscular action is thought to be responsible. The amount of force involved cannot be estimated. A true fracture, as contrasted with gradual weakening of structure from repeated mild traumata, cannot be differentiated roentgenographically.

LEWIS G. JACOBS, M.D.

Reduction in Height of the Last Lumbar Intervertebral Disc and the Occurrence of Lumbosacral Transitional Discs. Otto Wichtl. Fortschr. a. d. Geb. d. Röntgenstrahlen **62:** 229–247, October 1940.

The introduction to this paper describes the particular anatomic structure of the last lumbar vertebra and the last lumbar intervertebral disc, and emphasizes the particular stresses which these skeletal structures have to endure.

All intervertebral discs show physiologic changes with increasing age. These are particularly pronounced in the lumbar region and lead frequently to disease processes of the last disc—osteochondrosis. Concomitant secondary changes, especially involving the small intervertebral joints, are of importance. A reduction in the height of the last lumbar intervertebral disc is also observed in connection with various types of sacralization and lumbarization of the lumbosacral vertebral segments which, however, are to be regarded as physiologic processes of growth or retrogression, similar to those occurring in the sacral discs. For such physiologically low lumbosacral discs the designation lumbosacral transitional discs is proposed.

It is not certain at present whether or not such transitional discs occur without the presence of transitional lumbosacral vertebrae, as sufficient information concerning their formation and occurrence during the period of growth is not available. In children, transitional vertebrae have been demonstrated with certainty, but the possibility exists that these develop during the growth period; consequently, the observation of a low last disc in children with an otherwise normal vertebral column, cannot be interpreted with certainty as a lumbosacral transitional disc. The position of the promontory as occurring between the twenty-fifth and twenty-sixth vertebral segments in cases of lumbarization is mentioned.

The interpretation of low last lumbar intervertebral discs requires considerable caution. It is erroneous to consider them as definitely diseased in the presence of any type of sacralization, and they may even occur without such sacralization as developmental varieties.

H. A. JARRE, M D.

Osteomalacia, Osteoporosis, Osteopsathyrosis, Porotic Kyphosis. Robert Kienböck. Fortschr. a. d. Geb. d. Röntgenstrahlen **62:** 159–178, September 1940.

Osteoporosis and osteomalacia are related to low calcium content of bones, but represent quite different

anatomic changes and have to be classified separately. Microscopic investigations show that in osteoporosis cortex and spongiosa are thin but consist of normal lime-containing osseous tissue. In osteomalacia, however, the lime content is low and replaced to a varying degree by osteoid tissue, which finally renders these bones flexible and easy to cut. Microscopically, this differentiation as a rule is impossible. Bending of bones usually is the result of osteomalacia. Fractures result from osteoporosis. This is important for the roentgen differentiation, as multiple injuries and fractures are rather indicative of osteoporosis, especially osteopsathyrosis. In osteoporosis cortex and spongiosa give a clear-cut roentgenographic picture with smooth contours, while in osteomalacia structural detail is poor. Mixed forms of osteoporosis and osteomalacia, however, occur.

These osseous diseases exist in some localities as an endemic entity. Furthermore, they occur in larger numbers in circumscribed localities as the result of nutritional insufficiencies (hunger-osteopathy, hunger osteomalacia). Finally, sporadic cases are observed.

Referring to previous publications the author reviews a number of cases, partly from the literature, partly from personal observations, and tries to analyze briefly the relationship of these osseous deficiencies to endocrine disturbances, disease of the alimentary canal, especially endemic sprue, with some points for differential diagnosis, particularly in regard to multiple myeloma, multiple sarcomatous metastases, and osteitis fibrosa cystica.

Finally, porotic kyphosis is reviewed, with a report of several cases on the basis of which it is evident that this condition becomes decidedly more frequent with advancing age, affects women more frequently than men, and is particularly prone to develop as a result of enforced inactivity on whatever basis, together with faulty nutrition and aggravation of endocrine disturbances. Untreated, the disease leads to increasing kyphoscoliosis, with shortening of the trunk, collapse of vertebral segments, pain and stiffness, with formation of a diffuse osteoporosis, and multiple changes in the vertebral segments. Disturbances of the alimentary tract and increasing emaciation, however, are not encountered in this disease entity. A diet rich in vitamins, with addition of desirable endocrine preparations, and phosphorus, as well as calcium medication, is indicated. H. A. JARRE, M.D.

Albers-Schönberg Disease. Antonio Tunesi and F. Scolari. Radiol. med. **27:** 825–842, November 1940.

About 70 cases of Albers-Schönberg disease, or "marble bones," have been reported. The authors make an exhaustive study of these cases as well as of other conditions (anemia, polycythemia, etc.) that bring about sclerotic changes in the osseous tissue. The etiology they admit to be unknown. They believe, however, that there is a familial tendency.

Clinically the condition affects the young, and has been found even in stillborn and newborn infants. It would appear to be a congenital affliction that at times remains quiescent until later in life. The important symptoms are hyperchromic anemia and fragility of bone. In the adult the first sign may be a spontaneous fracture or the condition may be found accidentally during an x-ray examination. The nervous system may be affected and diminution of vision or complete blindness as well as diminished hearing may occur.

Progress varies with age in the adult; the patient may live many years after the discovery of the disease. In children the course is more severe and 75 per cent of the patients die as a result of the anemia or osteomyelitis with secondary septicemia.

The most important diagnostic data are furnished by the roentgenogram. Characteristic features are marked density of bone with disappearance of the medullary canal, due to sclerosis of the osseous tissue, a striated appearance of the shaft of the femur, humerus, or tibia, and thickening of the skull tables with density of the trabeculae in the intertabular space. The cranial foramina are quite often narrowed and the sella turcica may be small, causing symptoms referable to the cranial nerve.

Several excellent clinical histories are included, with excellent illustrations. A. MAYORAL, M.D.

Tuberculosis of the Spine: Observations on Localization, Extension and Healing—Their Bearing on Diagnosis and Treatment. J. V. de los Santos. Bull. Quezon Inst. **1:** 283–341, January 1941.

Seventy-four clinical cases of tuberculosis of the spine were examined roentgenologically. Twenty-one of the patients died and their spines were studied pathologically. The intervertebral articular type of disease was most common and the central type next in frequency. Pathological study showed multiple vertebral localization not demonstrated roentgenologically. The most common extension is toward the spinal canal and laterally or along the anterior and posterior spinal ligaments. The discs in children are less vulnerable then in adults. Sequestration is demonstrated with difficulty. Kissing sequestra apparently result from invasion of bone granulation tissue with intact intervertebral discs.

Repair is usually affected by fibrous tissue replacement. Osteoperiostitis, however, occurs in the region of the spinal ligaments and about the small intervertebral articulations. New bone formation about the ligaments and intervertebral joints is regarded as a contraindication for internal fixation.

WM. H. GILLENTINE, M.D.

Vertebral Hemangioma. L. Stehr. Fortschr. a. d. Geb. Röntgenstrahlen **62:** 179–188, September 1940.

This is a report of 14 cases of vertebral hemangioma, from the author's own practice. The characteristic appearance consists of a diminution in the number of vertical spongiosal trabeculae with concomitant condensation and thickening. This appearance is less conspicuous in the horizontal trabeculae.

Most of the cases were symptomless incidental observations. One patient with a transverse myelitis resulting from the hemangioma was subjected to laminectomy of the involved and two adjacent vertebrae. All paralysis disappeared in three years.

On the basis of two cases with trauma to the spine, it is assumed that the condensation and thickening of the remaining trabeculae produce such a consolidation that there is hardly a noticeable difference in the stability of the diseased vertebra as compared to the adjacent healthy ones. Operation on vertebrae involved by hemangioma did not produce any acceleration of tumor growth or further dissemination.

The roentgenographic appearance of vertebral hemangioma is regarded as so characteristic that erroneous diagnoses should no longer occur.

H. A. JARRE, M.D.

Periosteal Fibrosarcoma. Martin Batts, Jr. Arch. Surg. **42:** 566–576, March 1941.

The author reports 27 cases of periosteal fibrosarcoma. The tumor is relatively rare, constituting only about 1 case in every 8 primary bone tumors. Seventy-five per cent of the patients were under forty, and males were about twice as frequent as females. The predominant symptoms were pain and swelling, and the outstanding physical finding was a firm, deep-seated, smooth tumor not attached to the skin but fixed to the deep structures. The lesion is usually single and is most common in but not limited to the extremities. The roentgen

picture is of a large soft tissue mass with either lytic or reactive bone changes, lytic changes being more common. At operation the tumor is found to be encapsulated, but to involve the underlying bone.

Treatment in the author's series usually consisted of excision or amputation, roentgen therapy being given as an adjunct or when only palliation was anticipated. There were 40 per cent five-year survivals in a series of 27 patients. Death was usually due to pulmonary metastases; the grade of malignancy seemed to be the most important factor in deciding the outcome, as no patient with tumor graded 3 or 4 survived five years.

Some statistical analysis of the cases, not very complete, illustrates these points.

LEWIS G. JACOBS, M.D.

Calcification of the Supraspinatus Tendon: New Treatment. G. F. Dick, L. W. Hunt, and J. L. Ferry. J. A. M. A. **116:** 1202–1205, March 22, 1941.

Calcification of the supraspinatus tendon is a relatively common cause of pain and limitation of movement of the shoulder, occurring in adults of all ages, although it is most frequently found between the ages of thirty and forty-five. No cases have been reported among children. This condition is often erroneously diagnosed as bursitis, periarticular arthritis, brachial neuritis, paralysis of the radial nerve, or rheumatism. The cause of the calcification is unknown. The tendon is so situated that it is subject to frequent mild trauma by being pinched between the head of the humerus and the acromion. The deposit of calcareous material is occasionally encountered first in one shoulder and then in the other; in some persons the deposit undergoes absorption, while in others it persists. The pathologic picture is that of chronic inflammation; cultures from the deposits and the surrounding tissues have been reported negative for pathogenic organisms. Apparently the deposit of lime salts occurs quietly and precedes by a considerable interval the onset of the clinical symptoms.

The treatment that the authors have used with good results during the past few years consists of (1) relatively large doses of ammonium chloride, (2) rest of the diseased part, (3) physical therapy, (4) elimination of foci of infection.

C. G. SUTHERLAND, M.D.

RADIOTHERAPY

MALIGNANT CONDITIONS

Diagnosis and Management of Cancer of the Breast. A. C. Christie. Texas State J. Med. **36:** 722–728, March 1941.

The differential diagnosis of carcinoma of the breast is most difficult in the presence of a small movable tumor, chronic cystic mastitis, and a bloody discharge from the nipple. Transillumination may show a small movable tumor clear, in which case it is probably a simple cyst. In chronic cystic mastitis one is never sure that cancer is not present somewhere in the breast. A bloody discharge from the nipple means cancer in 50 per cent of the cases.

Palpation should be gentle; punch biopsy is to be avoided. Irradiation, 1,500 r in five or six days, is a valuable diagnostic aid. A radiosensitive cancer will become reduced in size or disappear in from ten days to two weeks. A less malignant carcinoma or benign growth remains stationary in size.

Physical examination with the patient seated upright may show the affected breast drawn upward slightly, slight dimpling, or slight retraction of the nipple. A scirrhous cancer at the lowermost margin of the breast, at its junction with the chest wall, may easily be overlooked.

The problems of treatment are even more difficult than those of diagnosis. If there is an element of uncertainty in a case of chronic cystic mastitis, cyst, or papilloma, there should be a course of preliminary roentgen therapy followed by resection and determination of the nature of the growth at the time of operation.

When a positive diagnosis can be made and the breast is operable, high-voltage preoperative irradiation, 2,500–3,000 r, with 2 mm. copper filtration, is given in two weeks using two overlapping fields. Operation follows six weeks after completion of the irradiation. Roentgen castration should be a routine procedure.

Contraindications to radical operation are youth and old age, rapid and complete response to irradiation, skin involvement, inflammation, ulceration, brawny induration, fixed or numerous axillary nodes, supraclavicular nodes, and distant metastases. Palliative irradiation is given with considerable benefit.

Statistics show 65 to 70 per cent clinical cures in early cases, by surgery; 4.5 to 16 per cent when there is definite clinical evidence of axillary node involvement; and 20 to 25 per cent cures as a whole.

JOHN M. MILES, M.D.

Inflammatory Cutaneous Metastatic Carcinoma. M. J. Reuter and R. Nomland. Wisconsin M. J. **40:** 196–201, March 1941.

The authors report four cases of inflammatory cutaneous metastatic carcinoma. In three of these the lesion was primary in the breast. In the fourth inflammatory metastasis developed in the skin of the neck from a cancer of the rectum.

The clinical features of inflammatory metastatic carcinoma of the skin are closely allied to erysipelas. As distinguished from true inflammation of the skin or erysipelas, however, there is no chill, fever, prostration, or leukocytosis. Clinically, the diagnosis is difficult and biopsy usually is required. Inflammatory signs developing in the skin on or about the breast which do not subside within two or three weeks warrant a biopsy for diagnosis. Pathologically, there is no true inflammation, but the invasion of lymph and blood vessels leads to marked congestion.

Irrespective of the form of treatment, the outlook for patients with this condition is extremely discouraging. In early cases surgery and roentgen irradiation should offer some hope. In advanced cases intensive roentgen therapy is rarely even palliative.

LESTER W. PAUL, M.D.

Two Cases of Bone Tumors (Multiple Myeloma and Plasmocytoma) Treated by Deep Therapy. Ignacio L. Alves Corrêa. Ann. paulist. de med. e cir. **40:** 461–487, December 1940; **41:** 3–22, January 1941.

The author reports two cases of bone tumor, one a multiple myeloma, the other a plasmocytoma, treated by deep roentgen therapy. After mentioning the technic used by others, he explains the method used in his cases as follows.

Fractional doses of 200 r were given through numerous ports until 2,000 r were given to the tumor during a period of six weeks, followed by a rest of from two to three months. The factors used were 200 kv., 3 mm. Al, and 0.5 mm. Cu.

The multiple myeloma received 4 such series of treatments at four-month intervals. Before the fourth or last series a profuse diarrhea developed, at times hemorrhagic, and pyuria, for which no definite cause was found. Death occurred from cachexia.

The plasmocytoma was in the right maxillary sinus. With the same factors as in the first case 2,000 r were administered to each of two fields, 200 r at each session.

Four months later another series of irradiation was given, the dose being reduced to 1,400 r per field for a total of 2,800 r. Complete disappearance of symptoms and regression of the tumor followed.

A. MAYORAL, M.D.

Retothelial Sarcomata Involving the Skull. W. Loepp. Fortschr. a. d. Geb. d. Röntgenstrahlen **62:** 211–229, October 1940.

So-called retothelial sarcomata—lymphosarcomata of the reticulo-endothelial system—have been recognized since 1930. They are to be differentiated from fibrosarcoma derived from the connective-tissue stroma of lymph nodes and from the endotheliomata, as well as lymphosarcomata of the lymph nodes. Theoretically, retothelial sarcoma could develop at any primary site of reticular tissue, but on the basis of collected statistics it is evident that these tumors involve predominantly the upper parts of the body. Thus 40 per cent arise in the tonsils, 20 per cent in the lymph nodes of the neck, axillae, mediastinum, and inguinal areas, while the remainder originate from the nasal pharynx, the nasal conchae, and the spleen. Only isolated cases were found involving the urinary bladder, uterus, stomach, small intestine, and skin.

The microscopic image shows a reticulated syncytial network of polymorphous, poorly defined and demarcated cells with numerous branchings. The nucleus has a distinct membrane; the chromatin is distributed in a dust-like manner. No intercellular substance is recognized A varying number of imbedded lymphocytes is present. Between the cells fibrillae are found which occasionally show a tendency toward collagen formation. Argentophil intraplasmal fibrillae, demonstrable by the staining method of Foot, are characteristic. Various degrees of maturity are observed.

Clinically, these tumors cannot be differentiated from other types of neoplasm, but recurrence of tumor tissue in the tonsillar fossae shortly after tonsillectomy and the occurrence of large lymph nodes in the neck following such operation will justify a suspicion of the neoplasm. Frequently enlarged cervical nodes are the first evidence of the disease. Surgery is entirely contraindicated, as it leads to rapid dissemination. Invasion of the cranial base is quite frequent. A number of roentgenograms illustrate this process.

Radiation therapy frequently leads to rapid initial reduction or disappearance of apparent neoplastic masses, but permanent cures evidently are quite rare. Intense fractionated irradiation of the nasopharynx, including the base of the skull and the entire neck, is recommended; also regular radiographic surveys of the base of the skull and the paranasal sinuses.

H. A. JARRE, M.D.

Carcinoma of the Cervix: Review of 200 Cases Treated with Radium. G. C. Wilkins. New England J. Med. **224:** 414–415, March 6, 1941.

Between the years 1920 and 1934, 200 cases of carcinoma of the cervix were treated by the author with radium only, using a single technic with only minor variations necessitated by circumstances. There were 185 primary carcinomas of the cervix and 15 carcinomas of the cervical stump. Thirty-seven per cent of the primary group and 20 per cent of the cervical stump group survived five years. In all cases diagnosis was confirmed by biopsy, which showed one adenocarcinoma one carcinoma of unidentified type, and 198 squamous-cell carcinomas. Classification is as follows; Stage I, 20 per cent with 63 per cent survival; Stage II, 11 per cent with 52 per cent survival; Stage III, 53 per cent with 35 per cent survival; Stage IV, 15 per cent with no survivals.

Usually 75 mg. of radium filtered through a 2 mm. brass screen was placed in the cervix, with another 2 mm. brass screen with 25 mg. of radium just above it, both being retained in place twenty-four hours. Two days later another application was made with 50 mg. in the canal and 50 mg. in the cross-arm, for eighteen hours. Three weeks later another application, like the first, was made for eighteen to twenty-four hours. Total irradiation amounted to 5,600 to 5,800 mg.-hr. In all treatments the vagina was packed with gauze in the usual manner. Since 1934, external irradiation by x-rays has been given, but these patients are not included in this report. JOHN MCANENY, M.D.

NON-MALIGNANT CONDITIONS

Rôle of Deep Therapy in Pruritus Vulvae. William E. Eastland. Southern M. J. **34:** 324–326, March 1941.

Superficial x-ray therapy is beneficially employed in the treatment of the common skin diseases affecting the vulva, as it is elsewhere in the body. In addition to irradiation it is advisable to apply vaseline or oil before defecation or urination and to cleanse and keep the parts dry thereafter.

For neurogenic or idiopathic pruritus vulvae deep x-ray therapy is advised. The author's method is to apply 200 r in air weekly, 2 mm. copper filtration, 200 kv., for three or four weeks, and then, if necessary, every two weeks to a total of 1,000–1,200 r. In a series of 7 cases he obtained marked benefit to the patients, superior to the results with superficial x-ray therapy. Technics used by others are listed.

JOHN M. MILES, M.D.

REACTIONS TO RADIATION

Studies in Radiation Sickness; Vitamins B_1 and C and the Small Intestinal Change in Radiation Sickness. William Stuart Wallace. Southern M. J. **34:** 170–173, February 1941.

Following heavy roentgen irradiation of the pelvis, small intestine changes similar to those seen in vitamin deficiency are found. The roentgen changes, in the ileum are segmentation of the barium stream, flattening of the mucosal pattern, diminution in motility, and narrowing of the lumen. Avitaminosis B_1 and C are already present in advanced carcinoma of the uterine cervix.

With these facts in mind, 5 patients with previously untreated cervical carcinoma were given daily intramuscular injections of 10 mg. thiamin chloride along with routine pelvic irradiation, while 5 others received daily doses of 50 mg. sodium ascorbutic acid (Lilly's cevalin). The irradiation was intensive, reaching 600 r daily, with either 400 kv. with a half value layer of 5 mm. copper or 200 kv. with a half value layer of 2 mm. copper. Each of 6 portals received 2,000 to 2,200 r total dosage and 8 patients received 2,500 to 5,000 r supplementary intravaginal radiation at 200 kv.

As a result of this study the author concludes that vitamin B_1 and C administration during heavy pelvic irradiation fails to diminish the occurrence or severity of diarrhea or to alter the radiographic changes in the ileum resulting from the irradiation. The ileal changes are apparently not due to lack of vitamin B_1 or C. Severe nausea and vomiting were, however, almost entirely eliminated by the vitamin B_1 and C administration.

JOHN M. MILES, M.D.